GALLAGHER & GALLAGHER, P.C.
120 2ND AVENUE
CHARLESTOWN, MA 02129-4533
617-598-3800
617-598-3900 (FAX)

DIRECT DIAL: 617-598-3801

OWEN GALLAGHER

April 5, 2001

VIA FEDERAL EXPRESS

U.S. Court of Federal Claims
Office of the Clerk
717 Madison Place, N.W.
Washington, DC 20005-1011

Re: **William H. Sweet, M.D. and Massachusetts Institute of Technology**
Vs: **The United States**
Nos. 00-274C & 00-292C

Dear Sir or Madam:

Enclosed for filing and docketing in the above-referenced matter please find an original and two copies of the following:

PLAINTIFF, MASSACHUSETTS INSTITUTE OF TECHNOLOGY'S RESPONSE TO UNITED STATES' MOTION TO DISMISS, IN PART, AND MOTION FOR PARTIAL SUMMARY JUDGMENT

AFFIDAVIT OF CAROLYN DULONG, MIT KEEPER OF THE RECORDS

AFFIDAVIT OF JOHN BERNARD, PH.D. REGARDING THE MIT NUCLEAR REACTOR AND THE PHYSICS OF BORON NEUTRON CAPTURE THERAPY

AFFIDAVIT OF MIT'S COUNSEL, OWEN GALLAGHER

PLAINTIFF, MASSACHUSETTS INSTITUTE OF TECHNOLOGY'S STATEMENT OF GENUINE ISSUES

PLAINTIFF, MASSACHUSETTS INSTITUTE OF TECHNOLOGY'S PROPOSED FINDINGS OF UNCONTROVERTED FACT

template 06C002 EKDS06C0

If you should have any questions, please do not hesitate to contact me.

Very truly yours,

Owen Gallagher
ogallagher@gallagherlaw.com

OG/smc
Enclosures

cc: David W. Odgen, Assistant Attorney General
David M. Cohen, Director
Brian M. Simkin, Senior Trial Counsel
John F. Cordes, Jr., Office of the General Counsel
Marjorie S. Nordlinger, Office of the General Counsel
Edward C. Jiran, Office of the General Counsel

Nos. 00-274C, 00-292C
(Judge Firestone)

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

WILLIAM H. SWEET, M.D.,

and

MASSACHUSETTS INSTITUTE OF TECHNOLOGY,

Plaintiffs,

v.

THE UNITED STATES,

Defendant.

PLAINTIFF, MASSACHUSETTS INSTITUTE OF TECHNOLOGY'S RESPONSE TO UNITED STATES' MOTION TO DISMISS, IN PART, AND MOTION FOR PARTIAL SUMMARY JUDGMENT

Owen Gallagher, Esquire
Kara Larzelere, Esquire
Gallagher & Gallagher, P.C.
120 2nd Avenue
Boston, MA 02129-4533
(617) 598-3800
Attorney for the Plaintiff
Massachusetts Institute of Technology

April 5, 2001

TABLE OF CONTENTS

TABLE OF AUTHORITES

Cases **Pages**

Statutes

Miscellaneous

INDEX TO APPENDIX

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

WILLIAM H. SWEET, M.D., and	)	
MASSACHUSETTS INSTITUTE OF TECHNOLOGY	)	
Plaintiffs	)	
	)	
v.	)	**Nos. 00-274C, 00-292C**
	)	**(Judge Firestone)**
THE UNITED STATES	)	
Defendant	)	

PLAINTIFF, MASSACHUSETTS INSTITUTE OF TECHNOLOGY'S RESPONSE TO UNITED STATES' MOTION TO DISMISS, IN PART, AND MOTION FOR PARTIAL SUMMARY JUDGMENT

The plaintiff, Massachusetts Institute of Technology ("MIT"), responds to the defendant's, the United States', Motion to Dismiss, in Part, and Motion for Partial Summary Judgment as follows.

STATEMENT OF THE QUESTIONS INVOLVED

1. Did the district court's finding that the complaint and allegations in Heinrich v. Sweet asserted public liability, and, therefore, that federal jurisdiction existed under Title 42, §2014(hh), establish, as a matter of law, that MIT defended a claim for public liability, indemnifiable under Title 42, §2210, where any public liability action under §2014(hh), is "deemed to be an action arising under §2210 of this title"?

2. Can the rights of MIT to an indemnity effective in 1960 and 1961, under the Price-Anderson Act, that would have indemnified MIT for its costs in defending claims for public liability that occurred in 1960 and 1961, be lost by a 1975 amendment to the

Price-Anderson Act that was not retroactive, because the claims based upon the 1960 and 1961 occurrences were not brought until discovered in 1995?

3. Where the United States entered into an indemnity agreement under the provisions of Title 42, §2210, that granted MIT an indemnity for defense costs in defending claims for public liability that occurred in 1960 and 1961, could a 1975 amendment to the Act affect MIT's contractual rights to be indemnified for defense of those claims that occurred before the amendment but that were brought after the amendment where the agreement was never amended to exclude the defense indemnity for such prior occurrences?

4. Does the Court have the authority to issue declaratory relief where such relief is "tied and subordinate to a monetary award"?

ARGUMENT

I. THE HEINRICH SUIT PRESENTED A "CLAIM FOR PUBLIC LIABILITY" AND THE COMMISSION MUST INDEMNIFY MIT FOR THE REASONABLE COSTS OF INVESTIGATING AND DEFENDING SUCH CLAIM.

Indemnity Agreement No. E-39 between MIT and the United States contains two separate and independent indemnity agreements. (Affidavit of Carolyn Dulong). The legal distinctions between these two undertakings of the government are critical to MIT's action.

Each separate indemnity is contained in Article III of the E-39 agreement. The first, in paragraph 1, states that:

> The Commission undertakes and agrees to indemnify and hold harmless the licensee and other persons indemnified, as their interest may appear, from public liability.

This provision only applies, if, and when, legal liability is established for a nuclear incident. In the underlying case of Heinrich, et al v. Sweet, et al., United States District Court for the District of Massachusetts, Civil Action No. 97-CIV-12134-WGY ("the Heinrich suit"), MIT was adjudged not liable. Thus, MIT does not seek any indemnity under this clause of the agreement.

The agreement also provides a separate indemnity for the reasonable costs of investigating and settling "claims for public liability." Specifically, Article III, paragraph 3 of the agreement provides:

> The Commission agrees to indemnify and hold harmless the licensee and other persons indemnified, as their interest may appear, from the reasonable costs of investigating, settling and defending **claims for public liability.** (emphasis added).

The MIT indemnity agreement defines "public liability" as "any legal liability arising out of or resulting from a nuclear incident" The agreement defines "nuclear incident" as:

> any occurrence or series of occurrences at the location or in the course of transportation causing bodily injury, sickness, disease or death or loss of or damage to property, arising out of or resulting from the radioactive, toxic, explosive or other hazardous properties of the radioactive material. Article I, para. 2(a).

Accordingly, the United States must indemnify MIT if the Heinrich suit presented claims for legal liability arising out of, or resulting from, any occurrence at the MIT reactor causing bodily injury or death arising out of, or resulting from, the radioactive, toxic, explosive, or other hazardous properties of the radioactive material. (See Affidavit of John Bernard, Ph.D.).

Whether there is "public liability" and whether there is a "claim for public liability" are, therefore, two separate questions. The only question that MIT has to answer is the latter. The former is simply irrelevant to this action as far as MIT is concerned.

A. The proposed reading of the indemnity by the United States regarding duty to indemnify defense costs is contrary to the rules of contract construction.

The government's basic proposition on contract construction regarding the defense cost indemnity is summed up by the statement on page 37, of its brief: "Plainly, because plaintiffs have not shown their responsibility for 'public liability,' they cannot demonstrate entitlement to indemnification for the costs of defending such claims."

Contrary to the position of the United States, a failure to demonstrate responsibility for "public liability" does not foreclose indemnity for costs in defending "claims for public liability".

Contract interpretation begins with the plain language of the agreement. *See* Gould, Inc. v. United States, 935 F.2d 1271, 1274 (Fed. Cir. 1991). A contract must be construed so as "to effectuate its spirit and purpose" and to give "reasonable meaning to all of its parts." Id. A contract is thus to be interpreted as a whole. *See* Granite Constr. Co. v. United States, 962 F.2d 998, 1003 (Fed. Cir. 1992). In the indemnity agreement, indemnification for "public liability" is differentiated from indemnification for "claims for public liability." The word "claims" must be accorded meaning.

B. The duty to indemnify costs of defending a claim of legal liability is broader, and independent of, the duty to indemnify a judgment of legal liability.

The legal issue raised by these two types of indemnity provisions has a long litigation history in the context of insurance law. Insurance policies that provide coverage for legal liability almost universally provide the same types of indemnity as provided in agreement No. E-39: a duty to defend an insured and a duty to indemnify the insured.

Courts have consistently held that a defense costs indemnity is broader, and independent of, the indemnity to pay judgments. Home Ins. Co. v. St. Paul Fire & Marine Ins. Co., 229 F.3d 56, 66 (2000) (1st. Cir.-Maine law) ("In contrast to the duty to defend, the duty to indemnify is narrower: while the duty to defend depends only on the allegations made against the insured, the duty to indemnify depends upon the facts established at trial and the theory under which judgment is actually entered in the case."); Brazas Sporting Arms, Inc. v. American Empire Surplus Lines Ins. Co. 220 F.3d 1, 4 (2000) (1st. Cir.-Massachusetts law) (" . . . , the duty to defend is broader than, and independent of, the duty to indemnify. . . . That is, the obligation to defend turns on the facts alleged in the complaint rather than the facts proven at trial."); Winnacunnet Cooperative School District v. National Union Fire Ins. Co. of Pittsburgh, PA, 84 F.3d 32, 35, n.6. (1996) (1st. Cir.-New Hampshire law); ("The duty to defend is broader than the duty to indemnify, as an insurer may be obligated to defend a groundless lawsuit that ultimately does not give rise to indemnification."); Commercial Union Ins. Assur. Co. v. Oak Park Marina, Inc., 198 F.3d 55, 59 (1999) (2nd. Cir-New York law) " . . . , an insurer's duty to defend is "exceedingly broad" and is separate from and more expansive than the duty to indemnify."); Stamford Wallpaper Co., Inc. v. TIG Insurance 138 F.3d 75, 79 (1998) (2nd. Cir-Conn. law) ("Where a complaint in an action . . . states a cause of action against the insured which appears to bring the claimed injury within the policy coverage, it is the contractual duty of the insurer to defend the insured in that action . . . regardless of the duty of the insurer to indemnify." [cite omitted]); New Castle County, Delaware v. National Union Fire Ins. Co. of Pittsburgh, PA, 174 F.3d 338, 343 (1999) (3rd. Cir.-Delaware. law) (". . . , an insurer is 'required to defend any action which potentially states a claim which is covered under the policy'."); First Oak Brook Corp. Syndicate v. Comly Holding Corp. 93 F.3d 92, 94-95 (1996) (3rd. Cir.-Pennsylvannia law) (". . .

an insurer is obligated to defend an insured whenever the complaint against its insured potentially may come within the policy's coverage.").

Similarly, here the obligation of the United States to indemnify MIT for the costs of defending a "claim for public liability" is broader than, and independent of, its obligation to indemnify MIT for "public liability."

C. The only issue for MIT is whether the Heinrich suit was a "claim for public liability" under the terms of the United States' separate undertaking to pay defense costs.

The operative issue for MIT's case is not whether there was, in fact, "public liability" as defined in Indemnity No. E-39 but, rather whether there was a "claim" for such liability. Obviously, this provides a legally broader base for indemnity since MIT's claim is only for defense costs.[1] MIT suggests that this issue has been determined by the Heinrich Court because of the 1988 amendments to the Price-Anderson Act.

D. The 1988 amendments to the Price-Anderson Act are dispositive of whether the Heinrich suit was a "claim for public liability."

In 1988, Congress enacted the Price-Anderson Amendments Act of 1988, Pub.L. No. 100-408, 102 Stat. 1066. MIT suggests that the provisions of this amendment, when coupled with the rulings of the district court under this amendment, resolve the issue of whether the Heinrich suit was a "claim for public liability."

1. Federal cause of action

[1] Naturally, MIT does not waive any additional indemnity claims, if the Heinrich plaintiffs should overturn on appeal the judgment in MIT's favor.

In the first instance, Congress created a new cause of action called a "public liability action." 42 U.S.C. § 2014(hh):

> The term "public liability action", as used in section 2210 of this title, means any suit asserting public liability. A public liability action shall be deemed to be an action arising under section 2210 of this title, and the substantive rules for decision in such action shall be derived from the law of the State in which the nuclear incident involved occurs, unless such law is inconsistent with the provisions of such section.

Congress also declared a "public liability action" to be a federal cause of action falling under the original and removal jurisdiction of the federal district court, ". . . without regard to the citizenship of any party or the amount in controversy." 42 U.S.C. §2210(n)(2).

Basically, the amended act provides a purely federal statutory scheme for all "public liability actions" that allege bodily injury resulting from radioactive or other hazardous properties of federally regulated nuclear materials. 42 U.S.C. §2014(hh). Such actions include "any legal liability arising out of or resulting from a nuclear incident", 42 U.S.C. §2014(w), where "nuclear incident" is defined broadly to encompass "any occurrence, including an extraordinary nuclear occurrence, within the United States causing, within or outside the United States, bodily injury, sickness, disease, or death." 42 U.S.C. §2014(q).

2. State law preemption

The result of the 1988 amendment was discussed by the Supreme Court in El Paso Natural Gas v. Neztososie, 526 US 473, n.6. (1999):

> This structure, in which a public liability action becomes a federal action, but one decided under substantive state law rules of decision that do not conflict with the Price-Anderson Act, . . ., resembles what we have spoken of as 'complete pre-emption' doctrine, . . ., under which 'the pre-emptive force of a statute is so 'extraordinary' that it 'converts an ordinary state common-law

> complaint into one stating a federal claim for purposes of the well-pleaded complaint rule,' "...

Additionally, courts have held that all state causes of action that could constitute a "public liability action" were preempted. Nieman v. NLO, Inc., 108 F.3d 1546, 1553 (6th Cir.1997) ([plaintiff] "can sue under the Price—Anderson Act, as amended, or not at all"); In re TMI Litigation II, 940 F.2d 832, 854 (3d Cir.1991) ("Congress clearly intended to supplant all possible state causes of action when the factual prerequisites of the statute are met.").

The result is that there is exclusive federal jurisdiction for this type of claim if, and only if, the allegations of the complaint fall within the definition of a "public liability action."

E. The United States is bound by the district court ruling that the Heinrich suit asserted public liability.

In the underlying Heinrich suit, MIT moved for partial summary judgment regarding the applicability of the Price Anderson Act to the plaintiffs' claims. Heinrich v. Sweet, 62 F.Supp.2d. 282, 295 (D.Mass. 1999).

To determine whether or not the Act applied, the Court presented to itself a threshold question: "does an indemnification agreement exist between the United States and the various private defendants that preemptively applies to the challenged conduct in this litigation?" Id. at 298. That is, do the plaintiffs' claims allege conduct by MIT and the other defendants that would preemptively be indemnified under the indemnity agreement? Id. The court added that, "If so, the Act will apply in this case, regardless of whether or not the indemnification agreement is later interpreted to reach the conduct of the private defendants." Id., at 298.

The court ultimately found that, "the challenged conduct in the instant litigation (with the exception of the alleged boron injections . . .) is subject to an indemnification agreement with the United States and therefore, the Price-Anderson Act applies to the plaintiffs' claims." Id., at 298.

It is important to note that since the 1988 amendments to Price-Anderson, district courts must make an initial determination that they have jurisdiction over a particular cause of action that is alleged to be a "public liability action." This determination necessarily requires a ruling on whether the claims alleged could possibly constitute a "nuclear incident."

MIT suggests to this Court that any such determination by the district court is binding as to the government's separate undertaking to pay defense costs on "claims for public liability." It is irrelevant to MIT's claim in this proceeding that the government may have the right to contest its ultimate indemnity when a judgment is rendered in any such action.

1. As a matter of law, the preliminary determination by the district court in Heinrich leads to the conclusion that a "claim for public liability" had been made against MIT.

When the district court determined that the Heinrich case was a "public liability action" because it asserted "public liability" under the Price-Anderson Act, the right of the government to contest that the suit was not a "claim for public liability" disappeared. The determination that a particular cause of action is a "public liability action" preempted by the Price-Anderson Act is peculiarly within the jurisdiction of the district court.

As a matter of law, the provisions of Title 42, §2014(hh), foreclose any argument by the government that the Heinrich complaint did not state a claim for public liability under indemnity No. E-39. Once the Heinrich court made its determination, §2014(hh) became the applicable law. In particular, the second sentence where it states:

A public liability action shall be deemed to be an action arising under section 2210 of this title, . . . (emphasis added).

Section 2210, of Title 42, is the provision that provides for the indemnity against public liability. Id. at 2210(k)(2) ("such contracts of indemnification shall cover public liability arising out of or in connection with the licensed activity.") The mandatory designation by Congress that public liability actions, once declared as such, are deemed to arise under §2210, is dispositive of the government's argument that the Heinrich claims did not relate to public liability.

2. The district court's reservation related to the ultimate duty of the NRC to indemnify any final judgments and did not affect its binding determination that the Heinrich suit was a "public liability action" under the Price-Anderson Act.

The district court in Heinrich stated that its ruling "does not bind any subsequent tribunal faced with the task of determining whether the United States in fact must indemnify a judgment rendered against MIT and/or Dr. Sweet." Heinrich at 298.

It is important to note that the district court's reservation was limited only to the indemnity for a final judgment. Whatever validity the district court's reservation may have had legally, the district court did not put any limitations on its ruling that a "claim for public liability" had been made against MIT.

The Heinrich court found, the alleged conduct by MIT claimed by the plaintiffs was subject to the indemnification agreement. Heinrich at 298. Therefore, MIT must be indemnified under the E-39 agreement for costs expended in investigating and defending the Heinrich claims.

The court was certainly aware that it was making a ruling that did have some legal effect. ". . . the Court must make a determination now regarding the applicability of the Act in order that the litigation proceed." Id. at 298. The determination that the court then made was a ruling

that the Heinrich action was a public liability action under Price-Anderson. Id. at 299. That order could only have been made where the court determined that the Heinrich complaint "asserted public liability."

The judicial decision that a suit asserts public liability is sufficient to dispose of the issue of whether a "claim for public liability" exists for which MIT is entitled to indemnity. This follows simply from the terms of §2014(hh) that puts a public liability action under §2210.

The effect of a district court's determination as to its jurisdiction over public liability actions is a double-edged sword. Would anyone believe, hypothetically, that if an indemnitee under Price Anderson brought an action for defense costs but could not show that it had defended a public liability action under §2014(hh) that it would have a valid claim for indemnity? The 1988 amendments have simply created a bright line jurisdictional test for whether defense costs are indemnified under Price-Anderson. If the indemnitee defends a public liability action, the costs are indemnified. If the indemnitee does not defend a public liability action, the costs are not indemnified.

F. The government was a party to this action when MIT claimed, and the judge ruled, that the Heinrich suit asserted public liability.

MIT would call this Court's attention to the fact that United States had an opportunity to be heard on whether the Heinrich suit was a public liability action when MIT presented its motion for partial summary judgment to the district court. In any event, it is MIT's position that the 1988 amendments to Price-Anderson vest the district court with exclusive jurisdiction to determine what is and what is not a public liability action. Once a district court rules that a

matter before it is a public liability action, that ruling is dispositive of applicability of the indemnity for defense costs under §2210. 42 U.S.C. §2014(hh).

II. THE HEINRICH CASE AROSE OUT OF A "NUCLEAR INCIDENT" AND THUS PRESENTS A "CLAIM FOR PUBLIC LIABILITY".

Notwithstanding the district court's ruling applying 42 U.S.C. §2014(hh), the United States contends that a "nuclear incident" did not occur and thus, it is not obligated to indemnify MIT. As argued above, MIT need not demonstrate that a nuclear incident occurred to recover under its indemnity claim, but need only show that the Heinrich suit asserted a claim for public liability. Id. Nevertheless, the plain language of the Price Anderson Act, the Commission's regulations and the MIT indemnity agreement all show that a "nuclear incident" did occur.[2]

The issue is whether the use of the MIT research reactor in connection with the 1961 BNCT trials constitutes a "nuclear incident." It does, if it was an "occurrence or series of occurrences at the location ... causing bodily injury, sickness, disease, or death ... arising out of or resulting from the radioactive, toxic, explosive, or other hazardous properties of the radioactive material."

Congress made the definition of "nuclear incident" intentionally broad, because it believed this was the best way to protect the public. In the words of the Senate Report accompanying the original enactment:

> The definition of "nuclear incident" is designed to protect the public against *any* form of damage arising from the special dangerous properties of the materials used in the atomic energy program. It includes *any* damage which may result from any hazardous property of source, special nuclear, or byproduct material. It includes bodily injury or death, loss of or damage to

[2] The following arguments were borrowed and adapted with permission from the brief of William H. Sweet.

property, and loss of use of property. While most incidents will be happenings which will be pinpointed in time - such as a runaway reactor or an inadvertent exposure to radiation - it was not thought that an incident would necessarily have to occur within any relatively short period of time. For instance, the steady exposure to radiation, such as from an undetected leak of radio-active materials from a storage bin, could constitute an incident.

S. Rep. 85-296, 1957 U.S. CODE CONG. & ADMIN. NEWS 1803, 1817 (emphasis supplied).

A. The Heinrich case arises from a "nuclear incident" within the plain language of the statute, the regulations, and the agreement.

The events giving rise to the Heinrich case unquestionably meet the broad statutory definition of a "nuclear incident." The plaintiffs allege, in the plainest possible terms, that their decedents suffered "bodily injury, sickness, disease [and] death" as a direct result of exposure to neutron beams generated by the MIT and Brookhaven reactors. Specifically, all four plaintiffs are alleged to have grown ill and died following, and because of, their Boron Neutron Capture Therapy ("BNCT"). This was the finding on autopsy for Heinrich and Sienkewicz (the other two apparently were not autopsied). More importantly, it was also the jury's finding.

Moreover, the neutron beam and the resulting effects (both therapeutic and destructive) of BNCT were produced by the "radioactive properties of the radioactive material." As the Affidavit of John Bernard explains:

> At MIT, the neutron beam used to initiate boron neutron capture therapy was generated from a radioactive isotope of uranium, Uranium-235, licensed to the MIT reactor by the Nuclear Regulatory Commission. (¶32)
>
> The neutron beam produced by the MIT reactor is caused by the radioactive properties of the nuclear source material that the MIT reactor is licensed to hold and use originally by the Atomic Energy Commission and subsequently by the Nuclear Regulatory Commission. (¶40)

Thus, although the Heinrich complaint is lengthy (79 pages) and multifarious (eleven counts asserting different legal theories), its thrust is simple: the plaintiffs allege that their decedents were fatally injured by nuclear radiation generated by the uranium core ("radioactive material") of the MIT and Brookhaven reactors. Their claims thus fit squarely within the statutory and contractual definition of a "nuclear incident."

The Court's analysis could - and should - stop there. When construing a statute, the Court's

> analysis begins with "the language of the statute." Where the statutory language provides a clear answer, the analysis ends there as well.... Ordinarily, an unambiguous statute, or one in which the plain meaning is clear from the words themselves, is conclusive. ... The plain meaning rule "tells a court what not to look at - legislative debates, committee reports, newspaper commentary.... The meaning of the law is what the words say it is."

Sullivan v. United States, 46 Fed. Cl. 480, 486 (2000) (citations omitted) (Horne, J.).

Applying unambiguous contract language is a similarly straightforward task:

> The court's examination begins with the plain language of the contract. If the contract language is unambiguous, the court's inquiry is at an end, and the plain language of the contract is controlling.

Input/Output Technology, Inc. v. United States, 44 Fed. Cl. 65, 70 (1999) (Firestone, J.), citing Textron Defense Systems v. United States, 143 F.3d 1465, 1469 (Fed. Cir. 1998) ("We ... first consider the language of the contract. Because the language is sufficiently clear, our inquiry ends there as well."). "The ordinary meaning of the language in contractual documents governs, and not a party's subjective but unexpressed intent. ... Moreover, the mere fact that the parties disagree upon the meaning of a contract does not render the language ambiguous." PCL Const. Services, Inc. v. United States, 47 Fed. Cl. 745, 785 (2000) (Horn, J.). "If a contract term

is unambiguous, the court cannot assign it another meaning, no matter how reasonable it may appear." Cray Research, Inc. v. United States, 41 Fed. Cl. 427, 435 (1998) (Weinstein, J.).

The language chosen by Congress and used in the indemnity agreement - "*any* occurrence or series of occurrences ..." - admits no exception. If Congress had intended to limit indemnity to cases involving reactor malfunction, or to except injuries resulting from medical applications or other purposeful uses of a reactor, as the United States now suggests, it could readily have done so. It did not, and as discussed below, there is no reason to think that Congress meant anything other than what it said.

B. The BNCT trials were not just "any type of incident somehow related to the operations of a licensed facility."

The United States observes that "under the plain terms of the agreement, Price-Anderson indemnification requires that the liability in question arise out of or result from a "*nuclear* incident, and not simply any type of incident somehow related to the operations of a licensed facility." (Defendant's Brief at 27-28; emphasis in original).

It would be hard to argue with this statement, as far as it goes. If the Heinrich plaintiffs had alleged a slip and fall on a wet floor at a nuclear plant, or a forklift accident, or a ceiling collapse, or an assault by a plant worker, or some other injury not caused by the "radioactive, toxic, explosive, or other hazardous properties of the radioactive material," there plainly would be no nuclear incident, and the statute and the agreement would not apply.

The United States takes a fanciful view of the facts, however, when it goes on to assert that "[t]he fact that a portion of the challenged conduct took place at a licensed nuclear facility was entirely inconsequential to the merits of the claims presented in *Heinrich*." (Defendant's

Brief, p. 29) Quite the contrary: all four plaintiffs' decedents received boron neutron capture therapy, which requires a slow neutron beam, which can *only* be generated by a nuclear reactor. None of the plaintiffs, in other words, found him/herself at a nuclear reactor by chance. And just as the reactor was integral to the treatment they were to receive, it is alleged to have been the cause of the injuries they suffered. It would be hard to envision a clearer case of alleged "bodily injury, sickness, disease, or death ... arising out of or resulting from the radioactive, toxic, explosive, or other hazardous properties of the radioactive material" - in short, a nuclear incident.

C. The Price-Anderson compensatory scheme is not limited to "unexpected nuclear reactor failures."

The United States, citing committee reports pertaining to Price-Anderson and various of its amendments, argues that Congress's paramount concern was the potentially vast liability that could result from "unexpected nuclear reactor failures, malfunctions, and the like." Because the reactors in this case performed as intended ("without incident"), the government argues there was no "nuclear incident" and therefore no indemnity.

To be sure, the legislative history of Price-Anderson and its amendments refers frequently to the possibility of a catastrophic reactor accident, and it was the possibility of such an event, and the fact that the potential damages exceeded the private insurance then available, that prompted Congress to pass the Act. By attempting to confine the Price-Anderson indemnity to such incidents, however, the United States does violence to the statutory language, the most fundamental tenets of statutory construction, and a substantial body of caselaw applying Price-Anderson to minor incidents, single-plaintiff cases, and cases where reactors performed as the operators intended and as federal regulations required.

1. Statutory language.

The language of the statute is discussed above. Here, it bears repeating only that a "nuclear incident" occurs *whenever* a person or property is injured by "the radioactive, toxic, explosive, or other hazardous properties of the radioactive material." That is what the statute says, and it nowhere requires that a "nuclear incident" be catastrophic, large, or even unexpected, for there to be indemnity.

Indeed, beginning with the 1966 amendments to Price-Anderson, Congress made special provision for "extraordinary nuclear occurrences," or "ENOs." An ENO is

> any event causing a discharge or dispersal of source, special nuclear, or byproduct material from its intended place of confinement in amounts offsite, or causing radiation levels offsite, which the Nuclear Regulatory Commission or the Secretary of Energy, as appropriate, determines to be substantial, and which the Nuclear Regulatory Commission or the Secretary of Energy, as appropriate, determines has resulted or probably will result in substantial damages to persons offsite or to property offsite.
>
> 42 U.S.C. §2014(j).

The 1966 amendments provided federal jurisdiction and removal power for cases arising out of ENOs. See In re TMI Litigation Consolidated Cases II, 940 F.2d 832, 853 n.18 (3d Cir. 1991), *cert. denied,* 503 U.S. 906 (1992). The 1988 amendments - passed in response to the Three Mile Island incident - further extended federal jurisdiction and removal to *all* nuclear incidents. See Id.

Even now, the Act continues to distinguish between ENOs, in which certain defenses are waived, 42 U.S.C. §2210(n), and all other "nuclear incidents." Significantly, however, while Congress has thus made special provision for the sort of large-scale nuclear catastrophes that members feared might overtax the available insurance pool, it has never *limited* Price-Anderson

indemnity to such disasters. To the contrary, "[t]he term 'nuclear incident' means *any* occurrence, *including an extraordinary nuclear occurrence,*" which meets the definitional requirement of injury or damage caused by "the radioactive, toxic, explosive, or other hazardous properties of the radioactive material." 42 U.S.C. §2014(q) (emphasis supplied).

In other words, had Congress wanted to limit Price-Anderson indemnity to catastrophic reactor accidents, as the United States now suggests, it certainly had the tools and the vocabulary to accomplish this. It did not do so, however, and neither should the Court.

2. Statutory Construction.

As noted above, the statutory definition of "nuclear incident" is plain on its face, and clearly covers the present case. "The meaning of the law is what the words say it is." Sullivan v. United States, *supra*. Committee reports and other legislative history are not needed to clarify what is already clear. Id.

The importance of *reading the statute* is well illustrated by the United States' argument that because Committee reports express concern about catastrophic nuclear accidents, the much broader statutory and contract definition of "nuclear incident" must not mean what it says. This is a bit like an insurance company saying that because a person purchased a homeowner's insurance policy primarily to cover a disaster (such as a fire), it must not cover minor claims (such as the theft of a camera). The obvious, and correct, reply is - don't try to read the insured's mind; read the insurance policy!

Of course, the words of a statute, *if* they are ambiguous, are to be interpreted in light of the statute's purpose. "But statutory prohibitions often go beyond the principal evil to cover reasonably comparable evils, and it is ultimately the provisions of our laws rather than the

principal concerns of our legislators by which we are governed." Oncale v. Sundowner Offshore Services, Inc., 523 U.S. 75, 79 (1998). Where the language chosen for the statute is broad, it is not the Court's function "to restrict the unqualified language of a statute to the particular evil that Congress was trying to remedy - even assuming that it is possible to identify that evil from something other than the text of the statute itself." Brogan v. United States, 522 U.S. 398, 403 (1998).

The bottom line is that Congress legislates by passing statutes, not by writing committee reports. While the possibility of a catastrophic accident may have been what animated the industry and members of Congress to do something, *what* it did was to pass comprehensive legislation whose meaning is plain, and which reaches the facts of this case. There simply is no reason not to do what the statute says.

3. Cases

Finally, any suggestion that only Chernobyl- or Three Mile Island-type accidents can be "nuclear incidents" under Price-Anderson is belied by the numerous reported cases under the Act. A few of these cases, in fact, *did* arise out of the Three Mile Island accident. Many others, however, have applied Price-Anderson to far more contained instances of environmental contamination or occupational exposure. In none of these cases (Three Mile Island excepted) was there a "major nuclear accident" (Defendant's Brief at 33), and none except TMI posed the threat of "extraordinarily extensive and, thus, uninsurable damage to the public" (Id. at 32). Yet Price-Anderson applied to all.

Nor must a "nuclear incident" be an accident at all. For example, several cases have held that a complaint by a nuclear plant worker, alleging occupational exposure to radiation, is

governed by Price-Anderson because it involves a nuclear incident, *even where the plaintiff does not allege a reactor accident, or even that his exposure exceeded the maximum levels permitted by federal regulations.* E.g., Roberts v. Florida Power & Light Co., 146 F.3d 1305 (11th Cir. 1998), *cert. denied,* 525 U.S. 1139 (1999); O'Conner v. Commonwealth Edison Co., 13 F.3d 1090, 1094-97, 1105 (7th Cir.), *cert. denied*, 512 U.S. 1222 (1994); Coley v. Commonwealth Edison Co., 768 F. Supp. 625 (N.D. Ill. 1991) (each holding that Price-Anderson conferred jurisdiction on the federal court and preempted contrary state law; because the plants complied with the standard of care supplied by federal regulation, the complaints were dismissed). In each of these cases the "reactor performed *without incident*" (to borrow the United States' pun at page 28 of its brief), yet a "nuclear incident" occurred within the meaning of 42 U.S.C. §2014(q), and Price-Anderson therefore applied.

These holdings do what the United States' brief does not: they follow faithfully the plain language of the statute. In each case, the plaintiff alleged injury, sickness and/or death resulting from the radioactive properties of the nuclear material used in the reactor - in short, a "nuclear incident" as the statute defines the term - and so Price Anderson applied. The Heinrich complaint likewise alleges injury, sickness and/or death resulting from the radioactive properties of the nuclear material used in the reactor, and so Price-Anderson applies here as well.

D. The BNCT trials, and the Heinrich plaintiffs' alleged injuries, constituted an "occurrence" as that term is used in the statute and the agreement.

The United States points to the word "occurrence" in the statute's and the agreement's definitions of "nuclear incident," and argues that this is "a term of art used in the insurance industry to specify an unexpected cause of loss," a synonym of "accident." Defendant's Brief at 30-31. Dr. Sweet's supposed "knowing decision to continue BNCT treatments after their

therapeutic value had ended," the government says, was not an "accident" or "occurrence," and so could not be a "nuclear incident." The United States fails to note any action by MIT that would preclude the claims against it from this supposed definition of occurrence.

The first difficulty with this argument is that it ignores the clear record that Congress intended that Price-Anderson indemnity should extend even to intentional acts. In fact, Congress expressly *rejected* a proposal by the AEC that intentional conduct be excepted from the indemnity provisions. The Senate Report explained:

> The suggestion which was contained in the original draft legislation of the [Atomic Energy] Commission that willful damages be excluded was not accepted since the damage to the public is the same, whether caused by any means - willful or nonwillful.

S. Rep. 85-296, 1957 U.S. CODE CONG. & ADMIN. NEWS at 1819.

Congress opted for a very broad definition of "nuclear incident" - extending even to intentional acts - so that an injured person's right to compensation would not be dependent on happenstance beyond that person's control. See Gilberg v. Stepan Co., 24 F. Supp. 2d 325, 335 (D.N.J. 1998) ("Price-Anderson guaranteed that compensation would be available to the public regardless of fault ....").

The government's "occurrence" argument is also wrong as a matter of simple historical fact. When Congress passed Price-Anderson in 1957, the word "occurrence" was not used in the insurance industry's standard form of liability policy; instead, the triggering event for insurance coverage under that form was an "accident." In Price-Anderson, however, Congress eschewed the term "accident" in favor of the term "occurrence." In ordinary English usage, an "occurrence" is something that happens, irrespective of cause; it "has a meaning much broader

than *accident.*" 16 E. Holmes, Holmes' Appleton on Insurance 2d §117.4 at 304 (2000). Congress's choice of words thus suited exactly its avowed intention to indemnify incidents "caused by any means - willful or nonwillful." (S. Rep. 85-296, *supra.*)

In 1966 - *nine years* after the passage of Price-Anderson - the insurance industry modified the standard form liability policy, so that the triggering event was now an "occurrence." R. Russ, et al., Couch on Insurance 3rd §126.25 at 126-48 to 126-49 (3d ed. 1999). This form also crafted the definition of "occurrence" that the United States quotes at p. 31 of its brief ("an accident, including a continuous or repeated exposure to conditions, which results in bodily injury or property damages neither expected nor intended from the standpoint of the insured").

Needless to say, the government's use of an industry term which (a) is narrower than ordinary English usage, and (b) came into being nine years after the statute being construed, is illogical, anachronistic, and completely unhelpful in determining what Congress meant in 1957.

However, even under the government's erroneous understanding of the statutory term "occurrence," there would be a "nuclear incident". "The definition of occurrence is generally met where the insured's conduct was reckless and not intentional," or where liability arises from the unintended consequences of an intentional act. 16 E. Holmes, Holmes' Appleton on Insurance 2d §117.4 at 311 (2000).

> It is only the intended injuries flowing from an intentional act that are excluded. ... If the consequences consisting of damages from intentional acts are not intended and are unexpected they are *accidental* within a policy of liability insurance.

Id. at 337, 339 (italics in original); see also the examples at pp. 339-40.

The judgment rendered in the Heinrich suit found MIT not liable on all counts against it. *Ergo,* it follows from this absolution of liability that the injury and death suffered by the Heinrich plaintiffs arising out of the exposure to the neutron beam therapy, was neither expected nor intended by MIT.

E. Price-Anderson does not exempt "nuclear medicine."

As the government interprets the legislative history, "it was Congress' intent to provide indemnification for uninsurable risks related to unexpected nuclear reactor failures, malfunctions, and the like, rather than general medical malpractice claims related to the practice of nuclear medicine." (Defendant's Brief at 33).

Nowhere in Price-Anderson, its legislative history, or the regulations and indemnity agreements implementing it is there any exemption for medical uses of reactors. As noted above, moreover, the legislative history confirms that even injuries that result from purposeful uses of reactors - not just "unexpected nuclear reactor failures, malfunctions, and the like" - are indemnified.

This is not, of course, to say that most malpractice claims involving nuclear medicine will be indemnified under Price-Anderson. Clearly, most are not, because medical procedures rarely take place on the premises of a licensed nuclear reactor ("at the location") as the regulations and indemnity agreement require, and they do not involve "radioactive material" as the statute defines the term. Such claims are therefore outside Price-Anderson, not because of some tacit "nuclear medicine" exemption, but because they fall outside the *express* definition of a "nuclear incident." See Gilberg v. Stepan Co., 24 F. Supp. 2d 325, 340-46 (D.N.J. 1998), discussed further below (application of Price-Anderson does not require that the release of

radioactivity be accidental, but does require "an 'event ... [at] "the location" or "the contract location" as defined in [an] indemnity agreement entered into pursuant to section 2210'"; nuclear medicine practiced in a hospital setting therefore is not subject to Price-Anderson).

The BNCT treatments that form the basis of the Heinrich case, on the other hand, *did* take place at a reactor ("location") covered by an indemnity agreement, and it resulted (the plaintiffs alleged, and the jury found) in injury, sickness and death caused by the radioactive properties of the nuclear material used in the reactor. What is more: medical uses, and BNCT in particular, were squarely within the parties' contemplation when the AEC issued the license for MIT-R, and when the parties entered into Indemnity Agreement E-39.

In the application materials submitted to the Commission, MIT revealed that one of the most important proposed intended uses of the MIT Reactor was to treat cancer patients. The application submission states in part:

> A facility is included in the MIT Reactor for irradiation of biological specimens, or patients. The main feature of this facility is a surgical operating room beneath the reactor. An opening in the concrete shielding allows a neutron and gamma ray beam to stream downward into the operating room. ... The neutron beam will be utilized in several different ways. Its most important use will be as a thermal neutron source for studies of cancer treatment in human patients.
>
> (Affidavit of Owen Gallagher, Ex. 4).

In January 1956, a Final Hazards Summary Report to the Commission's Advisory Committee on Reactor Safeguards states that the proposed MIT reactor facilities will be used to perform many types of experiments including, "The development of neutron beam therapy as a method of treatment of cancer, and other medical research." (Affidavit of Owen Gallagher, Ex. 1).

Prior to issuing the nuclear reactor facility license to MIT, the Commission prepared Proposed Findings and Conclusions in which it found, "The reactor is to be used for the conduct of research. Experimental facilities are provided for use in neutron diffraction work, horizontal beam experiments, **neutron beam therapy experiments,** exponential assembly experiments, and neutron irradiation studies. ... The experimental facilities ... consist of horizontal ports ... and a **medical therapy radiation facility**." (emphasis added). (Appendix, p. 2-3). Further, the Commission found, "MIT has submitted data describing the control and safety instrumentation and the administrative procedures relating to the use of the facility for **neutron beam therapy experiments and medical therapy.** The instrumentation and procedures appear to provide adequate protection for the health and safety of the public and personnel participating in the use of the facility for these purposes." (emphasis added). (Appendix, p. 2-3).

On or about June 8, 1958, the Commission issued License No. R-37 to MIT authorizing MIT to possess and operate a nuclear research reactor pursuant to sections 104(a) and 104(c) of the Atomic Energy Act of 1954. (Affidavit of Owen Gallagher, Ex. 2). Section 104(a) authorizes the Commission to issue licenses for utilization facilities for "**use in medical therapy**." Section 104(c) authorizes the Commission to issue licenses for utilization and production facilities useful in the conduct of research and development activities of the types specified in section 31. The research and development activities specified in section 31 include those relating to "utilization of special nuclear material and radioactive material for **medical,** biological, agricultural, health, or military purposes."

The license issued to MIT specifically states that, "Experimental facilities are provided for use in neutron diffraction work, horizontal beam experiments, **neutron beam therapy**

experiments, ... and neutron irradiation studies." (emphasis added). (Affidavit of Owen Gallagher, Ex. 2) The reactor was specially constructed with a surgical operating room on the premises. See diagram, Affidavit of Owen Gallagher, Ex. 5, p. 55-56.

Finally, the Commission was specifically aware of the proposed use of the reactor for Dr. Sweet's BNCT studies. On June 19, 1959, a task force from the Commission toured the MIT reactor with Dr. Sweet in connection with Commission contracts supporting his work. James F. Haggerty of the Commission's Medical Research Branch Division of Biology and Medicine reported to the Commission as follows:

> Dr. Sweet's work with boron in relation to brain tumor therapy has had some rough going. He has been pushing hard on the chemical side or boron containing organic compounds and Dr. Soloway brought us up to date on the compounds he has been working with. ... Dr. Sweet took us through the MIT reactor which has a medical port at the base of the reactor. We detected considerable disappointment with respect to ultimate functioning of the port for Dr. Sweet indicated it would be several months before he could treat his first patient in the reactor. Though the first patients will be brain tumor patients he mentioned he is thinking toward the possibility of irradiating the pituitary .... We completed our visit here with the feeling that this is an excellent research program and deserving of Commission support at the present level or possibly at an increased level.
>
> (Affidavit of Owen Gallagher, Ex. 3)

Use of the MIT reactor for experimental medicine, and for BNCT in particular, in other words, was not something the parties forgot about, or overlooked, or failed to anticipate, when they entered into the indemnity agreement. Given this fact and the facially broad definition of "nuclear incident," the failure to exempt medical applications explicitly in the indemnity agreement is striking - unless, of course, the intent was to make the agreement's coverage as broad as the record shows Congress intended it should be.

F. Case Law supports application of Price-Anderson to medical use of a reactor.

The Court has the benefit of several reported decisions that bear on Price-Anderson's application to medical uses of a reactor, beginning with Judge Young's thoughtful opinion in the private-party litigation that brings the parties to this Court. Heinrich v. Sweet, 62 F. Supp. 2d 282 (D. Mass. 1999) (referred to by the judge and counsel in that case as "Heinrich III"). In Heinrich, the plaintiffs argued, as the United States does here, "that 'nuclear incident' should only be interpreted to mean an unintended escape or release of nuclear energy." 62 F. Supp. 2d at 297.

In rejecting this argument, Judge Young cited four cases brought by or on behalf of employees or contractors, who alleged occupational exposure to radiation in the course of their work at nuclear power plants. Id., citing Day v. NLO, Inc., 851 F. Supp. 869, 876 (S.D. Ohio 1994) (Price-Anderson applies because "the Plaintiffs' intentional tort and negligence claims both arise from their alleged exposure to dangerous levels of radiation"); Sawyer v. Commonwealth Edison Co., 847 F. Supp. 96, 99-100 (N.D. Ill. 1994) (Act applies to claim for injuries resulting from alleged ongoing occupational exposure); Coley v. Commonwealth Edison Co., 768 F. Supp. 625 (N.D. Ill. 1991) (same); Building and Constr. Trades Dep't v. Rockwell Int'l, 756 F. Supp. 492, 494 (D. Colo. 1991), *aff'd,* 7 F.3d 1487 (10th Cir. 1993) (Act applies to intentional and negligent tort claims related to occupational exposure).

Also persuasive to Judge Young was Gilberg v. Stepan Co., 24 F. Supp. 2d 325 (D.N.J. 1998). There, the plaintiff alleged that his property was contaminated by a chemical plant that processed thorium, a radioactive metal used in the defendant's manufacture of iridescent gas mantles. The Gilberg court held that Price-Anderson did not apply to the facts before it, since

the torts alleged did not involve a licensed reactor that was subject to an indemnity agreement with the United States -- the touchstone of Price-Anderson coverage.

> To summarize, Price-Anderson sweeps broadly to include any claim alleging "public liability;" that is, "any legal liability arising out of or resulting from a nuclear incident." [42 U.S.C.] §2014(w). For there to be a nuclear incident, however, there must be an "occurrence," and an occurrence under the Act can only be an "event ... [at] 'the location' or 'the contract location' as defined in the applicable ... indemnity agreement, entered into pursuant to section 2210." [42 U.S.C.] §2014(j) & (q). No such agreement covers the Maywood chemical tailings.

24 F. Supp. 2d at 345-46.

In the course of a lengthy discussion of Price-Anderson and its implications (procedural and preemptive) for private-party litigation, the Gilberg court considered and rejected the argument that Price-Anderson applies only to the "unintended escape or release of nuclear energy."

> Price-Anderson ... neither requires that a nuclear source be used as intended nor requires that the escape or release of nuclear material be unintended. What Price-Anderson does require is that the escape or release occur in connection with indemnified activity.

Id. at 340. The court reached this conclusion based on the language of the statute, which contains no "unintentionality" requirement, and its legislative history - specifically, the fact that Congress in 1957 explicitly considered and rejected an exclusion for willfully caused releases. Id. at 335 & n. 9, 339-40, 345-46.

Both Heinrich III and Gilberg considered and rejected the Price-Anderson analysis of In re Cincinnati Radiation Litigation, 874 F. Supp. 796 (S.D. Ohio 1995), discussed at page 35 of the United States' brief. In Cincinnati, the plaintiffs alleged that cancer patients at Cincinnati General Hospital were exposed, without their knowledge or consent, to high doses of radiation in

order to study the likely effects of radiation on military personnel in the event of a nuclear attack. The court rejected the plaintiffs' count asserting an implied cause of action under Price-Anderson, holding that the Act did not apply to the facts of the case. A "nuclear incident," it held, occurs only when there is an "unintended escape or release of nuclear energy." 874 F. Supp. at 832.

As Gilberg pointed out, however, the Cincinnati court, in straying from the clear language of the statute, managed to "reach[] the correct result ... for the wrong reasons." The result was correct, not because Price-Anderson excludes intended releases, or nuclear medicine - both the statutory language and the legislative history say otherwise - but because Cincinnati did not involve "indemnified activity," i.e., the use of a licensed reactor that was the subject of an indemnity agreement with the United States. 24 F. Supp. 2d at 340.

Heinrich, however, is the case that Cincinnati was not: a nuclear incident resulting from the medical use of a licensed reactor which had a Price-Anderson indemnity agreement in place.

The government's obfuscatory efforts notwithstanding, this is at bottom a simple case. The statutory and contract definitions of "nuclear incident" are unambiguous, and they reach the facts of the case. There is no evidence that Congress meant to exclude medical or other intended uses of reactors from Price-Anderson indemnity; indeed, there is ample evidence to the contrary. The statute and the agreement mean what they say and say what they mean, and should be given effect.

III. THE HATHAWAY AMENDMENT DOES NOT AFFECT MIT'S RIGHT TO DEFENSE COSTS UNDER INDEMNITY E-39

When the government's brief is analyzed in the context of the district court's determination that the Heinrich case was a "public liability action" under the Price-Anderson Act most arguments become irrelevant. In fact, the only argument that remains as to MIT's claim for defense costs is the purported application of the Hathaway amendment. All other arguments relate to the question of ultimate indemnity and therefore do not apply to MIT's claim for defense costs.

A. The applicable indemnity agreement is the agreement in effect at the time of the occurrence.

Notwithstanding that the United States is a party to a contract, ordinary principles governing contracts and their interpretation remain applicable. See Lynch v. United States, 292 U.S. 571, 579 (1934). This principle was reaffirmed in United States v. Winstar Corp., 518 U.S. 839, 895 (1996). ("[W]hen the United States enters into contract relations, its rights and duties therein are governed generally by the law applicable to contracts between private individuals.")

The Indemnity Agreement No. E-39, dated May 13, 1964, is the applicable indemnity agreement. This agreement, "is effective as of 12:01 A.M., on the 9th day of June, 1958 and supersedes the interim indemnity agreement between the licensee and the Atomic Energy Commission dated May 25, 1959."

Article III, paragraph 5 of the E-39 agreement states:

> The obligations of the Commission under this agreement shall apply only with respect to nuclear incidents occurring during the term of this agreement.

While Article VII states:

> Termination of the term of this agreement shall not affect any obligation of the licensee or any obligation of the Commission under this agreement with respect to any nuclear incident occurring under the term of this agreement.

Each of these terms and the nature of the agreement itself would lead to a reasonable expectation that the Commission's obligations are governed by the agreement in effect at the time of the BNCT procedures conducted on the Heinrich plaintiffs in 1960 and 1961.

B. The United States has not overcome the presumption that the Hathaway amendment was prospective only.

The United States argues that the 1975 Hathaway Amendments to the Price Anderson Act which modified sections 170(c), (d) and (k) to exclude the cost of investigating, settling and defending claims from the aggregate indemnity voids Article III, paragraph 3 of the indemnity agreement providing indemnity for such costs.

First, there is no indication that Congress meant, in 1975, to take away indemnity rights pertaining to nuclear incidents which might have already occurred but were as yet undiscovered. The amendment states no effective date and has absolutely no statement that would indicate that it was intended to have retroactive effect.

As this Court has stated, "it is well settled that statues are presumed to operate prospectively unless express language in the statue provides otherwise." Ford v. United States, 33 Fed. Cl. 560, 565 (1995) (Robinson, J.), citing Bowen v. Georgetown University Hospital, 488 U.S. 204, 208-09 (1988) and United States v. Security Industrial Bank, 459 U.S. 70, 79-80 (1982). Where "nothing in the statute or legislative history suggests it was intended to be applied retroactively," a statute is to be applied prospectively. Id. *Accord,* People of the State of

California ex rel. Department of Transportation v. United States, 27 Fed. Cl. 130, 138 (1992) ("Because retroactivity is not favored in the law, congressional enactments and administrative rules will not be construed to have retroactive effect, absent specific mandatory language").

The presumption against statutory retroactivity is especially strong where the new provisions affect contractual rights in which predictability and stability are of prime importance. United States v. Security Industrial Bank, 459 U.S. 70, 79-82, 103 S.Ct. 407, 413-414, 74 L.Ed.2d 235 (1982).

The United States' argument - that Congress intended by the Hathaway Amendment to legislate retroactively and abrogate existing contractual rights pertaining to a nuclear incident which had occurred fourteen years earlier- simply breaks the accepted rules of contract and statutory construction.

Further, in support of its position, the United States notes that the Commission deleted the paragraph providing for indemnity of costs of defense from the form indemnity agreement applicable to nonprofit education licenses as it appears in the Commissions regulations. The amended regulation merely deletes the paragraph. It does not require the amendment of existing indemnity agreements. In addition, although the Hathaway Amendments to the Act were approved December 31, 1975, the Commission did not amend its regulations to reflect those amendments until more than eight years later on March 26, 1984.

The amended regulations specifically state an effective date of April 23, 1984, that would make them apply prospectively rather than retroactively. Therefore, even if the amended regulation required that existing agreements be amended to conform, which they do not, such

amendment would only be effective as of April 23, 1984. They certainly would have no legal effect on contractual provisions that apply to events that occurred in 1960 and 1961.

Further, the United States argues that even if the parties did not undertake to delete Article III, paragraph 3 from the MIT indemnity agreement, the deletion occurred by operation of law pursuant to the agreement of the parties. Article V of the MIT indemnity agreement states:

> The parties agree that they will enter into appropriate amendments of this agreement to the extent that such amendments are required pursuant to the Atomic Energy Act of 1954, as amended, or licenses, regulations or orders of the Commission.

As stated above, neither the Act nor the Commission's regulations *required* amendments to existing indemnity agreements. The enactment of the Hathaway Amendment did not automatically delete the paragraph since such a deletion required affirmative acts by the parties themselves. The parties agreed that they would enter into appropriate amendments to the extent required.

There are twelve amendments to the indemnity agreement. However, none of the amendments support the governments argument, since, by their own terms, they become effective after the date of the occurrences in question. The effective dates of the amendments range from January 1, 1966 to July 1, 1989. In fact, the parties amended the indemnity agreement three times between the passage of the Hathaway Amendment in late 1975, and the passage of the 1988 amendments to the Act. These amendments were by their numbers: number nine, effective May 1, 1977 (accepted, May 25, 1977); Amendment 10 effective May 1, 1979 (accepted, June 4, 1977); Amendment 11 effective May 1, 1977 (accepted, October 31, 1979). None of these three amendments, nor any prior or subsequent amendments, ever eliminated the

indemnity for defense costs contained in the E-39 agreement. The most recent amendment effective July 1, 1989, specifically adds an additional provision in a different section that indemnity shall include such legal costs of the licensee as are approved by the Commission.

The fact that the agreement continued to contain the indemnity indicates that the right to an indemnity for defense costs continued to apply to, at least, any events that had occurred before the Hathaway amendment. See Dupont v. U.S. 24 Fed. Cl. 635, 639 (1991).

IV. THIS COURT HAS JURISDICTION TO ENTER THE REQUESTED DECLARATORY JUDGMENT

The United States argues that this Court lacks jurisdiction over Dr. Sweet's and MIT's claims for declaratory relief. While it is certainly true that this Court does not have jurisdiction to issue a free-standing declaratory judgment, it *does* have authority to issue declaratory relief where such relief is "tied and subordinate to a monetary award." McKeel v. Islamic Republic of Iran, 722 F.2d 582, 591 (9th Cir. 1983), *cert. denied,* 469 U.S. 880 (1994); Alaska v. United States, 15 Cl. Ct. 276, 282-83 (1988); Ellis v. United States, 610 F.2d 760, 762 (Ct. Cl. 1979); Austin v. United States, 206 Ct. Cl. 719, 723, *cert. denied*, 423 U.S. 911 (1975).

In this case, MIT seeks indemnity for its defense costs - i.e., a monetary award - first and foremost. It seeks as well a declaration that the United States is obligated to indemnify it from future liability in cases arising out of the MIT BNCT trials. Such relief is "tied and subordinate to [the] monetary award" that MIT primarily seeks.

CONCLUSION

WHEREFORE, for the reasons stated above, the United States' Motion for Summary Judgment should be denied.

MASSACHUSETTS INSTITUTE OF TECHNOLOGY,
By its attorneys,

Owen Gallagher (BBO #183420)
Kara Larzelere (BBO #564941)
GALLAGHER & GALLAGHER, P.C.
120 2nd Avenue
Boston, MA 02129
617-598-3800

Dated: April 5, 2001

APPENDIX

EXHIBIT

ZN

Any interested person is invited to submit, within 30 days after publication of this notice in the FEDERAL REGISTER, evidence showing the practicability or impracticability of labeling fresh citrus fruit which has been treated after harvest with a chemical preservative, with the name of each chemical preservative ingredient at time of retail sales. Comments should be submitted in quintuplicate to the Hearing Clerk, Room 5440, Department of Health, Education, and Welfare Building, 330 Independence Avenue SW., Washington 25, D. C.

Dated: March 31, 1958.

[SEAL] GEO. P. LARRICK,
Commissioner of Food and Drugs.

[F. R. Doc. 58-2495; Filed, Apr. 3, 1958; 8:49 a. m.]

NOTICES

DEPARTMENT OF COMMERCE

Bureau of Foreign Commerce

[File 7-60, 23-565]

INDUSTRIE-WARENVERKEHR AND GEORG EIGLER

ORDER FURTHER EXTENDING ORDER TEMPORARILY DENYING EXPORT PRIVILEGES

In the matter of Industrie-Warenverkehr, and Georg Eigler, Liliengasse 1, Vienna, Austria, respondents; File 7-60, 23-565.

Upon the application of the Investigation Staff of the Bureau of Foreign Commerce and, it appearing that the Agent-in-Charge, Investigation Staff, has commenced a proceeding against the respondents for an order denying to them all privileges of participating in exportations from the United States by reason of their conduct in connection with the unauthorized transshipment of 100 tons of tetraethyl lead originally exported from the United States to Austria as the place of ultimate destination and, it further appearing that the respondents admit their participation in such unauthorized transshipment and acquiesence in the temporary order heretofore issued against them.

It is ordered, That the order of December 17, 1957 (22 F. R. 10310) temporarily denying export privileges to Industrie-Warenverkehr and Georg Eigler, heretofore extended on February 14, 1958 until March 31, 1958, be, and the same hereby is further extended until the completion of the said proceeding and the entry of a final order determining the same.

Dated: April 1, 1958.

JOHN C. BORTON,
Director,
Office of Export Supply.

[F. R. Doc. 58-2490; Filed, Apr. 3, 1958; 8:48 a. m.]

Federal Maritime Board

SHEPARD STEAMSHIP CO. ET AL.

NOTICE OF TERMINATION OF BAREBOAT CHARTERS

Notice of annual review of bareboat charters covering the vessels "John M. Boseman", "Thomas Paine", and "Samuel F. Miller" (Charterers: Shepard Steamship Company, American Coal Shipping, Inc., and Boston Shipping Corporation, respectively), appeared in the FEDERAL REGISTER issue of March 28, 1958 (23 F. R. 2081), in which comments were invited with respect to justification for continuing or discontinuing said charters.

The Federal Maritime Board has determined that conditions do not exist justifying the continuance of the charters beyond a year's period of operation of the vessels named above.

Dated: April 2, 1958.

By order of the Federal Maritime Board.

[SEAL] JAMES L. PIMPER,
Secretary.

[F. R. Doc. 58-2530; Filed, Apr. 3, 1958; 8:58 a. m.]

Office of the Secretary

CURT OHEIM

STATEMENT OF CHANGES IN FINANCIAL INTERESTS

In accordance with the requirements of section 710 (b) (6) of the Defense Production Act of 1950, as amended, and Executive Order 10647 of November 28, 1955, the following changes have taken place in my financial interests as reported in the FEDERAL REGISTER of September 25, 1956, 21 F. R. 7301; March 29, 1957, 22 F. R. 2093; October 1, 1957, 22 F. R. 7777.

A. Deletions: No change.
B. Additions: No change.

This statement is made as of March 19, 1958.

Dated: March 24, 1958.

CURT OHEIM.

[F. R. Doc. 58-2475; Filed, Apr. 3, 1958; 8:45 a. m.]

VERN I. MCCARTHY, JR.

STATEMENT OF CHANGES IN FINANCIAL INTERESTS

In accordance with the requirements of section 710 (b) (6) of the Defense Production Act of 1950, as amended, and Executive Order 10647 of November 28, 1955, the following changes have taken place in my financial interests as reported in the FEDERAL REGISTER of September 26, 1956, 21 F. R. 7351; March 29, 1957, 22 F. R. 2093; 22 F. R. 7777.

A. Deletions: None.
B. Additions: Delta-f, Inc., Hoffman International Corp., Triune Holdings Co.

This statement is made as of March 14, 1958.

Dated: March 27, 1958.

VERN I. MCCARTHY, Jr.

[F. R. Doc. 58-2476; Filed, Apr. 3, 1958; 8:45 a. m.]

MORLAN J. GRANDBOIS

STATEMENT OF CHANGES IN FINANCIAL INTERESTS

In accordance with the requirements of section 710 (b) (6) of the Defense Production Act of 1950, as amended, and Executive Order 10647 of November 28, 1955, the following changes have taken place in my financial interests as reported in the FEDERAL REGISTER of April 12, 1957, 22 F. R. 2512; October 8, 1957, 22 F. R. 8008.

A. Deletions: No change.
B. Additions: No change.

This statement is made as of March 26, 1958.

Dated: March 26, 1958.

MORLAN J. GRANDBOIS.

[F. R. Doc. 58-2477; Filed, Apr. 3, 1958; 8:45 a. m.]

CLARENCE BLUMOEHR

STATEMENT OF CHANGES IN FINANCIAL INTERESTS

In accordance with the requirements of section 710 (b) (6) of the Defense Production Act of 1950, as amended, and Executive Order 10647 of November 28, 1955, the following changes have taken place in my financial interests as reported in the FEDERAL REGISTER of April 28, 1956, 21 F. R. 2795; October 2, 1956, 21 F. R. 7553; April 11, 1957, 22 F. R. 2441; October 10, 1957, 22 F. R. 8072.

A. Deletions: No change.
B. Additions: No change.

This statement is made as of March 22, 1958.

Dated: March 22, 1958.

CLARENCE BLUMOEHR.

[F. R. Doc. 58-2478; Filed, Apr. 3, 1958; 8:45 a. m.]

ATOMIC ENERGY COMMISSION

[Docket No. 50-20]

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

NOTICE OF PROPOSED ISSUANCE OF FACILITY LICENSE

Please take notice that the Atomic Energy Commission proposes to issue a facility license to Massachusetts Institute of Technology substantially in the form set forth in Annex "B" unless within thirty (30) days after filing of this notice

with the Federal Register Division a request for formal hearing is filed with the Commission in accordance with the Commission's rules of practice (10 CFR Part 2). There is included as Annex "A" the proposed findings and conclusions concerning the proposed license. The proposed license would authorize Massachusetts Institute of Technology to operate the nuclear research reactor at the site described in its application for license. Construction of the facility was authorized by Construction Permit No. CPRR-5 issued on May 7, 1956 (21 F. R. 3150). Prior to issuance of the license the facility will be inspected by representatives of the Commission to determine whether it has been constructed in accordance with the terms and conditions of the construction permit.

For further details see (1) the application submitted by Massachusetts Institute of Technology, and amendments thereto; (2) a report dated January 13, 1958, from the Chairman, Advisory Committee on Reactor Safeguards, to the Chairman, Atomic Energy Commission, reporting as to the Committee's review of the application, as amended, and (3) a memorandum dated March 27, 1958, submitted by the Director, Division of Licensing and Regulation, which summarizes the principal safety factors considered in reviewing the application for license, all on file at the Commission's Public Document Room, 1717 H Street, NW., Washington, D. C.

Dated at Germantown, Md., this 31st day of March 1958.

For the Atomic Energy Commission.

H. L. PRICE,
Director,
Division of Licensing and Regulation.

ANNEX "A"

PROPOSED FINDINGS AND CONCLUSIONS

A. *Proposed findings.* 1. On February 20, 1956, the Massachusetts Institute of Technology (hereinafter referred to as MIT) submitted an application for the necessary licenses to construct and operate a research reactor.

2. MIT is a nonprofit, private educational institution organized under the laws of the State of Massachusetts. MIT is not owned, controlled, or dominated by an alien, foreign corporation, or foreign government.

3. The MIT reactor is a one megawatt (thermal) heavy water-cooled and -moderated, heterogeneous, enriched uranium reactor. The reactor is to be used for the conduct of research. Experimental facilities are provided for use in neutron diffraction work, horizontal beam experiments, neutron beam therapy experiments, exponential assembly experiments, and neutron irradiation studies.

The reactor core and the heavy water moderator are contained in an aluminum pressure vessel. The experimental facilities located outside of the pressure vessel in the graphite reflector, consist of horizontal ports, rotary changing ports, instrument ports, pneumatic tube changers, thimble tubes, thermal columns, and a medical therapy radiation facility. The only experimental facilities located inside of the pressure vessel are six small sample tubes in the heavy water moderator.

The fuel consists of 19 curved plate-type fuel elements, similar to those in the Materials Testing Reactor at Arco, Idaho.

For control and regulation of the reactor, there are six top entry shim-safety rods which penetrate vertically through seals in the pressure vessel into the core region. The control rod drive mechanisms are located between two concrete plugs at the top of the reactor tank.

The pressure vessel for this reactor is an aluminum cylinder 4 feet in diameter and ¼ inch thick. This vessel was designed to be in accordance with the ASME Code for Unfired Pressure Vessels to withstand a pressure of 40 psig. The top lid of the pressure vessel is designed to withstand 80 psig. The pressure vessel is surrounded by two feet of graphite. The graphite is enclosed in a boral-lined steel gas-tight container. Outside of this container is a water-cooled thermal shield consisting of a layer of steel and lead. Surrounding the thermal shield is a layer of high density concrete about six feet thick which serves as the biological shield.

The coolant system consists of a primary heavy water loop heat exchanger, a secondary light water loop, and a cooling tower in the secondary loop. The coolant pipes enter at the bottom of the pressure vessel and circulate upward through the core.

4. On May 7, 1956, the AEC issued Construction Permit No. CPRR-5 to MIT for the construction of the reactor for which they are now seeking an operating license.

5. The construction permit CPRR-5 provided that "MIT is financially qualified to construct and operate the reactor in accordance with the regulations contained in Title 10, Chapter I, Code of Federal Regulations; to assume financial responsibility for the payment of Commission charges for special nuclear material and to undertake and carry out the proposed use of such material for a reasonable period of time." There has been no information developed with respect to the financial qualifications of MIT which significantly changes the facts upon which this conclusion was based.

6. The Massachusetts Institute of Technology has had many years experience in conducting a program of instruction and experimentation in the field of nuclear engineering and related subjects. The MIT staff is well trained in the theoretical aspects of reactor operation and several members of the staff have had operating experience with reactors.

7. The construction permit specified certain additional information required of the applicant prior to the issuance of the operating license. Such information included:

(a) A standard operating procedure, including start-up routine and non-routine operation, and shut-down;

(b) A description of critical experiments to be performed, including procedures to be followed; and

(c) A plan of action for disaster control in event of an accident or incident resulting in a radioactive hazard to the public.

Information on these matters has been supplied and is discussed in Findings Number 8, 9, and 10, respectively.

8. During the initial start-up, the reactor coolant system is to be filled with light water and flow tests are to be conducted using primarily dummy fuel elements. After these tests are completed, the fuel elements are to be removed and the reactor is to be drained, dried and then filled with heavy water. Checks are then to be made to insure that all operating conditions, instrumentation and controls, experimental facilities, and safety systems are in proper order.

The reactor is to be operated five days per week. At the beginning of each operating period all safety systems are to be checked and, if necessary, a new fuel element is to be loaded. Each time a new loading has been made, an experiment is to be performed to determine the critical position of shim and control rods.

The applicant has established operating rules for this facility including administrative regulations for routine and emergency procedures, procedures for reviewing reactor experiments, and procedures for determining the qualification and responsibilities of operators. The proposed operating procedures appear to be adequate to provide reasonable assurance that the reactor can be operated safely.

9. MIT is to conduct a number of initial critical experiments including calibration of shim rods, regulating rod, heavy water level, and neutron absorbers; oscillation frequency experiments; reactivity experiments involving non-uniform loadings, neutron flux and spectral distribution measurements; radiation surveys; fission product poisoning measurements; instrumentation adjustments and calibrations; temperature distribution measurements; temperature and void coefficient measurements; and general performance, inspection, checks and tests with simulation of possible failures. The experiments described and the means for conducting such experiments appear adequate to provide the necessary initial operating data.

10. MIT has established a detailed disaster control plan. This plan provides for the evacuation of people under the immediate control of MIT and for immediate liaison, where necessary, with appropriate State and local officials. This plan appears adequate to provide for emergency situations.

11. The reactor is located in a steel containment building. The building has been designed in accordance with the American Petroleum Institute Recommended Rules for Large Welded Low-Pressure Storage Tanks to withstand an internal pressure of 1 psi. A concrete shadow shield 2 feet thick and 33 feet high surrounds the interior of the containment building.

The containment building is penetrated by a personnel air-lock, a truck air-lock, an inlet air duct, an aluminum neutron window, a hot-plug storage tank, two hydraulic lifts, an exhaust air duct, an emergency escape air-lock and several pipes and conduits. MIT is providing in both the inlet and outlet lines of the ventilation system for an automatically controlled valve, and a manually operated valve in series.

The control mechanisms provided at the points of penetrations in the containment building and the nature and frequency of proposed leakage tests appear adequate to provide reasonable assurance that the leakage rate specified will be maintained. The leakage of the building will be measured after all penetrations have been installed and there will be annual tests for leak tightness.

The construction permit approved the substitution of a single steel door in place of the truck air-lock in the containment building subject to two conditions. These conditions are not relevant, since MIT has constructed the reactor with the truck air-lock. The air-lock is adequate.

12. The MIT reactor is generally similar to the CP-5 research reactor at Argonne National Laboratory and should exhibit similar characteristics. Negative temperature and void coefficients and a long neutron lifetime, which are characteristics of a reactor of this general design concept, provide a high degree of inherent stability.

The temperature and void coefficients are expected to be sufficiently negative to assure safe operation. However, the information on which this finding is based consists of theoretical calculations. The sign and magnitude of these coefficients cannot be definitively established until measurements are made during actual operation of the reactor.

13. The maximum credible accident for this facility consists of the instantaneous insertion of not more than 2.3 percent excess reactivity. MIT has stated that such an insertion of excess reactivity could be caused by dropping a fuel element into the central fuel element position in the core of the reactor. The initiating mechanisms for this accident would require a combination of circumstances the concurrent occurrence of which are highly improbable.

The instantaneous insertion of 2.2 percent excess reactivity would place the reactor on a period of approximately 40 milliseconds. Based on the postulated thermal characteristics and temperature coefficient values for the MIT reactor, the temperature reached in the fuel is calculated to be well below the melting point of the fuel. The resulting excursion would be terminated by inherent shutdown characteristics of the core itself before any significant damage would result to the reactor.

Based upon information presently available, the acceptance of this accident as the maximum credible accident is dependent upon a limitation of the amount of excess reactivity which can be inserted by the loss of a single experiment. MIT has calculated that the amount of excess reactivity which could be added to the reactor as a result of flooding all of the experimental facilities with light water would be approximately 1 percent. Such flooding could credibly occur concurrently with the loss of a single experiment.

14. The greatest possible release of fission products under the conditions of containment specified for this facility from accidental spillage in the handling of the largest experiment to be conducted in this facility would be considerably less than 1.5 r of gamma radiation and an integrated dose of 92 rep to the thyroid from iodine 131 to a person continuously exposed at the site boundary for one hour. While a release of sufficient magnitude to result in such exposures is highly unlikely, these doses would not result in any clinically observable damage to those exposed.

15. MIT has submitted data describing the control and safety instrumentation and the administrative procedures relating to the use of the facility for neutron beam therapy experiments and medical therapy. The instrumentation and procedures appear to provide adequate protection for the health and safety of the public and personnel participating in the use of the facility for these purposes.

16. On January 27, 1958, MIT filed with the Commission, as proof of financial protection pursuant to 10 CFR Part 140, copies of binder No. 14, issued by Mutual Atomic Energy Liability Underwriters, covering this facility in the amount of $2,000,000.

17. The application has been referred to the Advisory Committee on Reactor Safeguards for a report with respect to the hazards of the facility. The report of the Committee has been made available to the public.

18. The AEC staff and the Commission's Advisory Committee on Reactor Safeguards believe that the MIT reactor can be operated with an acceptable degree of risk to the health and safety of the public. The advisory Committee recommended that provision be made for an auxiliary system of closing the inlet and outlet lines of the ventilation system. Since the ACRS considered this matter, MIT has provided an adequate manually operated valve which is auxiliary to the automatically controlled valve already proposed.

B. *Proposed conclusions.* 1. The processes to be performed, the operating procedures, the facility and equipment, the use of the facility and other technical specifications provide reasonable assurance that the applicant will comply with the regulations in Chapter 1 of Title 10 of the Code of Federal Regulations, including the regulations in Part 20, and that the health and safety of the public will not be endangered by the operation of this facility, subject to the following conditions:

(a) No experiment shall be introduced into or permitted to remain in the reactor if more than one percent excess reactivity would be introduced into the reactor by the withdrawal or loss of that experiment.

(b) The reactor shall not be operated at a power level in excess of that necessary to measure the temperature and void coefficients until MIT has measured these coefficients and found them to be of the sign, and substantially of the magnitude, calculated in its application.

2. MIT is technically qualified to operate the proposed reactor.

3. MIT is financially qualified to operate the reactor in accordance with the regulations contained in Title 10, Chapter 1, of the Code of Federal Regulations, and to assume financial responsibility for the payment of Commission charges for special nuclear material and to undertake and carry out the proposed use of such material for a reasonable period of time.

4. MIT has submitted proof of financial protection which satisfies the requirements of Commission regulations which are currently in effect.

5. The issuance of a license will not be inimical to the common defense and security or to the health and safety of the public.

For the Atomic Energy Commission.

——— ———,
Director,
Division of Licensing and Regulation.

ANNEX "B"

PROPOSED LICENSE

License No.

1. Subject to the conditions and requirements incorporated herein, the Commission hereby licenses Massachusetts Institute of Technology (hereinafter referred to as "MIT"):

a. Pursuant to section 104a and c of the Atomic Energy Act of 1954 as amended, and Title 10, CFR, Chapter I, Part 50, "Licensing of Production and Utilization Facilities", to possess and operate as a utilization facility the nuclear research reactor facility (hereinafter "the facility") designated below;

b. Pursuant to the act and Title 10, CFR, Chapter 1, Part 70, "Special Nuclear Material", to receive, possess and use 12 kilograms of uranium enriched to approximately 93 percent in the uranium 235 isotope as fuel for operation of the facility;

c. Pursuant to the act and Title 10, CFR, Chapter I, Part 30, "Licensing of Byproduct Material", to possess, but not to separate, such byproduct material as may be produced in the operation of the facility.

2. This license applies to the facility which is owned by MIT and located in Cambridge, Massachusetts, and described in MIT's application filed on February 20, 1956, and amendments to the application, filed on May 13, 1957, September 16, 1957, November 27, 1957, January 2, 1958, January 9, 1958, January 27, 1958, February 24, 1958, and March 25, 1958 (hereinafter "the application").

3. This license shall be deemed to contain and be subject to the conditions specified in § 50.54 of Part 50 and § 70.32 of Part 70; is subject to all applicable provisions of the act and rules, regulations and orders of the Commission now or hereafter in effect; and is subject to the additional conditions specified or incorporated below.

a. *Operating restrictions.* (1) MIT shall operate the facility in accordance with the procedures and limitations described in the application.

(2) MIT shall not operate the facility at a power level in excess of 1,000 kilowatts (thermal).

(3) No experiment shall be introduced into or permitted to remain in the reactor if more than one percent excess reactivity would be introduced into the reactor by the withdrawal or loss of that experiment.

(4) The reactor shall not be operated at a power level in excess of that necessary to measure the temperature and void coefficients until MIT has measured these coefficients and found them to be of the sign, and substantially of the magnitude, calculated in its application.

b. *Records.* In addition to those otherwise required under this license and applicable regulations, MIT shall keep the following records:

(1) Facility operating records, including power levels.

(2) Records showing radioactivity released or discharged into the air or water beyond the effective control of MIT as measured at the point of such release or discharge.

(3) Records of emergency scrams, including reasons for emergency shutdowns.

c. *Reports.* (1) MIT shall immediately report to the Commission any indication or occurrence of a possible unsafe condition relating to the operation of the facility.

(2) MIT shall, upon completion of the start-up experiments described in its application, submit a report to the Commission describing such experiments and the results thereof.

4. Pursuant to § 50.60 of the regulations in Title 10, Chapter I, CFR, Part 50, the Commission has allocated to MIT, for use in the operation of the reactor, 11.63 kilograms of uranium 235 contained in uranium (enriched to approximately 93 percent in the isotope uranium 235). Estimated schedules of special nuclear material transfers to MIT and returns to the Commission are contained in Appendix "A" which is attached hereto. Shipments by the Commission to MIT in accordance with column 2 in Appendix "A" will be conditioned upon MIT's return to the Commission of material substantially in accordance with column 3 of Appendix "A".

5. This license is effective as of the date of issuance and shall expire at midnight May 7, 1996 unless sooner terminated.

Date of issuance:

For the Atomic Energy Commission.

——— ———,
Director,
Division of Licensing and Regulation.

APPENDIX "A" TO MASSACHUSETTS INSTITUTE OF TECHNOLOGY FACILITY LICENSE

ESTIMATED SCHEDULE OF TRANSFERS OF SPECIAL NUCLEAR MATERIAL FROM THE COMMISSION TO MASSACHUSETTS INSTITUTE OF TECHNOLOGY AND TO THE COMMISSION FROM MIT

(1)	(2)	(3)		(4)	(5)
Date of transfer (fiscal year)	Transfers from AEC to MIT, kgs. U-235	Returns by MIT to AEC, kgs. U-235: Recoverable cold scrap	Returns by MIT to AEC, kgs. U-235: Spent hot fuel	Net yearly distribution including cumulative losses, kgs. U-235	Cumulative distribution including cumulative losses, kgs. U-235
1957	5.00			5.00	5.00
1958	1.04	3.04	0.92	(2.92)	2.08
1959	3.33	1.66	1.37	0.30	2.38
1960	2.50	1.25	1.00	0.25	2.63
(1)	(1)	(1)	(1)	(1)	(1)
1996	2.50	1.25	1.00	0.25	11.63
Inventory to be returned			2.23	(2.23)	9.40
	101.87	50.95	41.52	9.40	

[1] In years 1960 through 1996, columns (2) through (4) carry the same quantities. Column (5) increases by 0.25 kg. each year.

[F. R. Doc. 58-2494; Filed, Apr. 3, 1958; 8:48 a. m.]

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

WILLIAM H. SWEET, M.D., and MASSACHUSETTS INSTITUTE OF TECHNOLOGY Plaintiffs v. THE UNITED STATES Defendant	))))))))	Nos. 00-274C, 00-292C (Judge Firestone)

PLAINTIFF, MASSACHUSETTS INSTITUTE OF TECHNOLOGY'S STATEMENT OF GENUINE ISSUES

The plaintiff, Massachusetts Institute of Technology ("MIT"), responds to the Defendant, the United States' Proposed Findings of Controverted Fact as follows:

1. Admitted. However, MIT refers the Court to document cited which speaks for itself.

2. MIT admits that on or about April 16, 1959 that its license was amended to exempt MIT as a nonprofit educational institution from the financial protection requirements of section 170a of the Price-Anderson Act. Nevertheless, MIT maintained nuclear energy liability insurance through the Mutual Atomic Energy Underwriters (MAELU) in the amount of $250,000.

3. Admitted. However, MIT refers the Court to document cited which speaks for itself.

4. Admitted. However, MIT refers the Court to document cited which speaks for itself.

5. Admitted. However, MIT states that although Indemnity Agreement No. E-39 is dated May 13, 1964, it states that it is effective as of June 9, 1958 and that it supersedes the interim indemnity agreement between the licensee and the AEC.

6. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

7. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

8. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

9. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

10. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

11. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

12. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

13. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

14. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

15. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

16. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

17. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

18. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

19. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

20. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

21. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

22. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

23. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

24. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

25. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

26. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

27. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

28. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

29. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

30. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

31. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

32. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

33. Admitted. However, MIT refers the Court to the document cited which speaks for itself.

34. MIT states that the document cited speaks for itself.

35. Admitted. MIT further states that Owen Gallagher by his letter of August 28, 1999, notified Ms. Nordlinger that on August 16, 1999, the judge presiding over the Heinrich case issued a Memorandum and Order ruling that the Price-Anderson Act applied to certain claims in the action and notifying Ms. Nordlinger that a jury was

scheduled to be impaneled in the case on September 7, 1999. MIT refers the Court to the document cited which speaks for itself.

36. Admitted. However, MIT refers the Court to the decision cited which speaks for itself.

37. MIT states that the document cited speaks for itself.

38. MIT states that the document cited speaks for itself.

39. MIT states that the document cited speaks for itself.

40. MIT states that the document cited speaks for itself.

41. Admitted. However, MIT refers the Court to the Jury Verdict which speaks for itself.

42. MIT states that the document cited speaks for itself.

43. Admitted. However, MIT refers the Court to decision cited which speaks for itself.

44. Admitted. However, MIT refers the Court to decision cited which speaks for itself.

45. Admitted. However, MIT refers the Court to decision cited which speaks for itself.

46. Admitted. However, MIT refers the Court to the document and decision cited which speak for themselves.

47. Admitted. However, MIT refers the Court to documents cited which speak for themselves.

In addition to the above, MIT states that in the event that this Court does not find that the court's ruling in the underlying matter of Heinrich v. Sweet is dispositive on the issue of whether the Heinrich suit presented "claims of public liability", a genuine issue of material fact remains as to whether the BNCT trials at the MIT reactor constituted a "nuclear incident" for the purposes of the indemnity agreement. For example, see the accompanying Affidavit of John Bernard, Ph.D. attesting to the nuclear reaction resulting from the interaction of neutrons produced from the source material contained in the MIT reactor with boron-10 contained within the cellular structures of the Heinrich claimants. Affidavit of John Bernard, Ph.D., paragraph 41.

MASSACHUSETTS INSTITUTE OF TECHNOLOGY,
By its attorneys,

Owen Gallagher (BBO #183420)
Kara Larzelere (BBO #564941)
GALLAGHER & GALLAGHER, P.C.
120 2nd Avenue
Boston, MA 02129
617-598-3800

Dated: April 5, 2001

KL;C:\AMIPRO\DOCS\ACTIVE\MIT\350SGI.SAM;04/05/2001

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

WILLIAM H. SWEET, M.D., and **MASSACHUSETTS INSTITUTE OF TECHNOLOGY** **Plaintiffs**	)))	
v.	)))	**Nos. 00-274C, 00-292C** **(Judge Firestone)**
THE UNITED STATES **Defendant**	))	

PLAINTIFF, MASSACHUSETTS INSTITUTE OF TECHNOLOGY'S PROPOSED FINDINGS OF UNCONTROVERTED FACT

The plaintiff, Massachusetts Institute of Technology ("MIT"), asserts additional proposed findings of uncontroverted fact as follows:

History of the MIT Reactor - Licensing and Indemnity

1. In 1956, MIT submitted an application for the necessary licenses to construct and operate a nuclear research reactor. (Appendix, p. 2-3).

2. In the application materials submitted to the Commission, MIT stated that one of the most important proposed intended uses of the MIT Reactor was to treat cancer patients. The application submission states in part:

> A facility is included in the MIT Reactor for irradiation of biological specimens, or patients. The main feature of this facility is a surgical operating room beneath the reactor. An opening in the concrete shielding allows a neutron and gamma ray beam to stream downward into the operating room. ... The neutron beam will be utilized in several different ways. Its most important use will be as

a thermal neutron source for studies of cancer treatment in human patients. (Affidavit of Owen Gallagher, Ex. 4).

3. In January 1956, a Final Hazards Summary Report to the Commission's Advisory Committee on Reactor Safeguards states that the proposed MIT reactor facilities will be used to perform many types of experiments including, "The development of neutron beam therapy as a method of treatment of cancer, and other medical research." (Affidavit of Owen Gallagher, Ex. 1).

4. On May 7, 1956, the Commission issued Construction Permit No. CPRR-5 to MIT for the construction of the reactor. The construction permit provided that, "MIT is financially qualified to construct and operate the reactor in accordance with the regulations ..., to assume financial responsibility for the payment of Commission charges for special nuclear material and to undertake and carry out the proposed use of such material for a reasonable time." (Appendix, p. 2-3).

5. Prior to the issuance of the facility license to MIT, the Commission made Findings and Conclusions. The proposed findings and conclusions were posted in the Federal Register, on April 4, 1958. (Appendix, p. 2-3).

6. The Commission found that MIT "has had many years experience in conducting a program of instruction and experimentation in the field of nuclear engineering and related subjects. The MIT staff is well trained in the theoretical aspects of reactor

operation and several members of the staff have had operating experience with reactors." (Appendix, p. 2-3).

7. The Commission further found that, "The reactor is to be used for the conduct of research. Experimental facilities are provided for use in neutron diffraction work, horizontal beam experiments, **neutron beam therapy experiments,** exponential assembly experiments, and neutron irradiation studies. ... The experimental facilities ... consist of horizontal ports ... and a **medical therapy radiation facility**." (emphasis added). (Appendix, p. 2-3).

8. Further, the Commission found, "MIT has submitted data describing the control and safety instrumentation and the administrative procedures relating to the use of the facility for **neutron beam therapy experiments and medical therapy.** The instrumentation and procedures appear to provide adequate protection for the health and safety of the public and personnel participating in the use of the facility for these purposes." (emphasis added). (Appendix, p. 2-3).

9. On January 27, 1958, MIT filed with the Commission as proof of financial protection pursuant to 10 C.F.R., Part 140, copies of binder No. 14, issued by Mutual Atomic Energy Liability Underwriters, covering this facility in the amount of $2,000,000. The Commission concluded that, "MIT has submitted proof of

financial protection which satisfies the requirements of the Commission regulations which are currently in effect." (Appendix, p. 2-3).

10. On or about June 8, 1958, the Commission issued License No. R-37 to MIT authorizing MIT to possess and operate a nuclear research reactor pursuant to sections 104(a) and 104(c) of the Atomic Energy Act of 1954. (Affidavit of Owen Gallagher, Ex. 2).

11. Section 104(a) authorizes the Commission to issue licenses for utilization facilities for "**use in medical therapy**." (emphasis added).

12. Section 104(c) authorizes the Commission to issue licenses for utilization and production facilities useful in the conduct of research and development activities of the types specified in section 31. The research and development activities specified in section 31 include those relating to "utilization of special nuclear material and radioactive material for **medical,** biological, agricultural, health, or military purposes". (emphasis added).

13. The license issued to MIT states that it is licensed pursuant to Section 104(a) - "use in medical therapy" and Section 104(c) for facilities in the conduct of research including medical research. The license states that it applies to the facility owned by MIT and notes specifically that, "Experimental facilities are provided for use in neutron diffraction work, horizontal beam experiments, **neutron beam therapy**

experiments, ... and neutron irradiation studies." (emphasis added). (Affidavit of Owen Gallagher, Ex. 2).

14. The license also authorizes MIT to "receive, possess and use 12 kilograms of uranium enriched to approximately 93% in the uranium 235 isotope as fuel for operation of the facility". (Affidavit of Owen Gallagher, Ex. 2).

15. The Commission was specifically aware of the proposed use of the reactor for Dr. Sweet's Boron Neutron Capture Therapy studies. On June 19, 1959, a task force from the Commission toured the MIT reactor with Dr. Sweet in connection with Commission contracts supporting his work. James F. Haggerty of the Commission's Medical Research Branch Division of Biology and Medicine reported to the Commission as follows:

> Dr. Sweet's work with boron in relation to brain tumor therapy has had some rough going. He has been pushing hard on the chemical side or boron containing organic compounds and Dr. Soloway brought us up to date on the compounds he has been working with. ... Dr. Sweet took us through the MIT reactor which has a medical port at the base of the reactor. We detected considerable disappointment with respect to ultimate functioning of the port for Dr. Sweet indicated it would be several months before he could treat his first patient in the reactor. Though the first patients will be brain tumor patients he mentioned he is thinking toward the possibility of irradiating the pituitary .... We completed our visit here with the feeling that this is an excellent research program and deserving of Commission support at the present level or possibly at an increased level.
>
> (Affidavit of Owen Gallagher, Ex. 3)

16. By letter dated May 25, 1959, and accepted by MIT on or about August 1, 1959, the Commission and MIT entered into an interim indemnification agreement "with respect to such public liability as arises out of or in connection with the activity licensed under AEC License No. R-37." (MIT's Complaint, Ex. A).

17. The letter of May 25, 1959, was, per its terms, later superseded by a formal Indemnity Agreement No. E-39. (MIT's Complaint, Ex. A).

18. Indemnity Agreement No. E-39 is dated May 13, 1964 and states that it "is effective as of 12:01 A.M., on the 9th day of June, 1958 and supersedes the interim indemnity agreement between the licensee and the Atomic Energy Commission dated May 25, 1959." (Affidavit of Owen Gallagher, Ex. 2).

19. The indemnity agreement provides:

> The Commission undertakes and agrees to indemnify and hold harmless the licensee and other persons indemnified, as their interest may appear, from public liability.
>
> (Affidavit of Owen Gallagher, Ex. 2, Article III, paragraph 1).

20. The agreement also provides:

> The Commission agrees to indemnify and hold harmless the licensee and other persons indemnified, as their interest may appear, from the reasonable costs of investigating, settling and defending claims for public liability.
>
> (Affidavit of Owen Gallagher, Ex. 2, Article III, paragraph 3).

21. This indemnity agreement, as amended, is still in effect today. (Affidavit of Carolyn Dulong).

22. There are twelve (12) amendments to the indemnity agreement. The effective dates of the amendments range from 1966 to 1989. (Affidavit of Carolyn Dulong).

23. The amendments indicate that Article III, paragraph 3 of the indemnity agreement regarding indemnity for the costs of investigating, settling and defending claims for public liability was never amended or deleted. (Affidavit of Carolyn Dulong).

MASSACHUSETTS INSTITUTE OF TECHNOLOGY,
By its attorneys,

Owen Gallagher (BBO #183420)
Kara Larzelere (BBO #564941)
GALLAGHER & GALLAGHER, P.C.
120 2nd Avenue
Boston, MA 02129
617-598-3800

Dated: April 5, 2001

KL;C:\AMIPRO\DOCS\ACTIVE\MIT\350PF.SAM;04/05/2001

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

WILLIAM H. SWEET, M.D., and **MASSACHUSETTS INSTITUTE OF TECHNOLOGY** **Plaintiffs** v. **THE UNITED STATES** **Defendant**	))))))))	**Nos. 00-274C, 00-292C** **(Judge Firestone)**

AFFIDAVIT OF JOHN BERNARD, PH. D. REGARDING THE MIT NUCLEAR REACTOR AND THE PHYSICS OF BORON NEUTRON CAPTURE THERAPY

I, John Bernard, Ph.D. aver:

1. I am the director of the Nuclear Reactor Laboratory at the Massachusetts Institute of Technology in Cambridge, Massachusetts. I have held this position since June, 1999. In this position I am responsible for the scientific direction and management of the reactor laboratory.

2. I began my employment at the MIT Research Reactor in 1975, as a reactor operator. Since that time I have been continuously employed at the reactor and have held the positions of Reactor Operator (3/75 - 6/76), Senior Shift Supervisor (6/76 - 8/79), Reactor Superintendent, 8/79 - 6/88), Director of Reactor Operations (this is the senior licensed position at MIT) 6/88 - present), and Interim Director (10/96 - 6/99).

3. I have also held a position as Principal Research Engineer in the MIT Department of Nuclear Engineering since July, 1990.

4. I hold a Ph.D. in Nuclear Engineering from the Massachusetts Institute of Technology. I have the additional professional education and expertise in the area of nuclear engineering and in particular boron neutron capture therapy as specified in my curriculum vitae which is attached hereto and incorporated herein by reference as Exhibit "A".

5. I am familiar with the theory and practice of boron neutron capture therapy from the viewpoint of nuclear physics. I have actual participation in the planning of boron neutron capture therapy treatments that were conducted at the reactor in the early 1990's.

6. The theoretical underpinnings for boron neutron capture therapy go back to 1936.

7. The first theoretical description of what was to be called boron neutron capture therapy was first published in 1936 in the American Journal of Roentgenology. G. Locher, "Biological Affects And Therapeutic Possibilities Of Neutrons," 1936, 36:-1-13. This publication was only four years after the discovery of the neutron.

8. While since 1936, there have been a number of advances in neutron sources and in boron bearing compounds that are used in boron neutron capture therapy the underlying physics of the procedure is similar to that which was first described by Locher.

9. The basic concept arose from the fact that brain tumors were generally not treatable. In particular, they were not treatable by drugs because the brain's blood barrier insulated it from any foreign substances. They were also not treatable effectively by radiation because the tumor was in the brain.

10. Boron, however, was one element that had the property that it could pass through the brain's blood barrier.

11. Additionally, brain tumors also absorbed certain boron compounds in a substantially greater ratio than healthy cells.

12. The ability of boron compounds to pass into the brain and be disproportionately absorbed by tumor cells coupled with some unique nuclear properties of boron led to the scientific conclusion that boron neutron capture therapy might allow for highly specific and highly localized radiation doses to be used to kill brain tumors.

13. The particular nuclear properties that made boron uniquely suitable for treating brain cancers require only some basic nuclear physics.

14. All matter at the nuclear level can be considered for the purposes of boron neutron capture therapy to be composed of three basic building blocks: protons, neutrons and electrons. Naturally, there are many more basic particles. A basic explanation of the nuclear physics underlying boron neutron capture therapy, however, can be given without involving too many other particles or theoretical terms.

15. Both protons and electrons are electrically charged particles. Protons have a positive electrical charge and electrons have a negative electrical charge. Neutrons have no charge but they do bind to protons in atomic nuclei through the operation of the so-called "strong force". The nature of the strong force is not material to this affidavit except insofar as it is the mechanism by which protons and neutrons are joined in atomic nuclei.

16. The generally accepted table of elements catalogs matter by the number of protons contained within its atomic nuclei. For example, hydrogen has a nucleus composed of one proton and is placed in number one in the table of elements. Helium has two protons in its nucleus and is classified as element number two. The naturally occurring elements proceed in this classification from one, hydrogen, to 92, uranium. With uranium having

92 protons in the nucleus of its atom.

17. The elements involved in boron neutron capture therapy are elements numbers 2,3 and 5: helium, lithium and boron, respectively.

18. Generally, the number of protons and electrons in the atomic nuclei of a given element are the same in number. This results in an electronically neutral atom. Occasionally, the number of electrons in certain nuclei are less than the number of protons. When this occurs such atoms are considered to be "ionized."

19. Ionized particles have the potential to cause secondary ionization by acquiring electrons from other atoms. Ionized particles that are formed within organic bodies can be especially damaging since secondary ionization (electrons of the elements of the compound losing electrons) can cause the breakdown of organic compounds within the cells and cause cell death.

20. The nuclei of all atoms, other than hydrogen, have neutrons as an additional component.

21. Since neutrons have no discernable electrical charge, there may be the same or more or less neutrons in an atomic nucleus than there are protons.

22. The specific number of neutrons that combine with the fixed number of protons in the nuclei of a given element creates what is called an "isotope" of an element.

23. The various isotopes of an element are identified in written form by placing the total number of protons and neutrons contained in the isotope's nucleus following the name of the element. For example, boron-10 is what is generally called boron. It is, however, an isotope of boron, even though it has 5 protons and 5 neutrons in its nuclei. Boron-11 is also an isotope of boron. It is identified as boron-11 because it has 6, and not 5, neutrons in its nucleus along with the requisite 5 protons.

24. Accordingly, isotopes of an element are simply atomic nuclei of a specific element that have the requisite number of protons and electrons but have a definite number of neutrons which may equal the number of protons or be greater (or, in some instances, less) than the number of protons.

25. Many isotopes of elements occur naturally in nature. One well-known example is carbon-14, a naturally occurring radioactive isotope of carbon (carbon-12). Since the rate of radioactive decay for carbon-14 is known, its residual amount can be used in dating organic matter. The use of this technique beginning approximately fifty years ago revolutionized archaeology and paleontology.

26. Many theoretically possible isotopes of elements are simply not found in nature because there atomic nuclei are unstable. The instability manifests itself through the mechanism known as "radioactivity."

27. A generally accepted definition of radioactivity is a "spontaneous nuclear transformations that result in the formation of new elements". H. Cember, Ph.D., "Introduction To Health Physics," McGraw Hill Health Professions Division, 3rd ed., p 75.

28. These spontaneous nuclear transformations may be accomplished by one of several different mechanisms, including alpha-particle emission,[1] beta particle emission,[2] , positron emission,[3] and orbital electron capture.[4]

29. The most important of these mechanisms for boron neutron capture therapy is alpha-particle emission. Alpha-particle emission is another name for is what more commonly called nuclear fission. An alpha-particle is an ionized helium atom. It is ionized because it has no electrons and consists entirely of two protons and two neutrons with the two protons having positive electric charges.

30. The nuclear transformation occurs in the element that emits the alpha-particle (helium atom) from its nucleus. When the alpha-particle is emitted, the number of protons in the nucleus is immediately reduced by two. This results in the formation of a new element or elements.

31. To initiate boron neutron capture, a neutron beam, generated by a nuclear reactor, is aimed at boron-10, which is the basic isotope of boron, containing 5 protons and 5 neutrons.

32. At MIT, the neutron beam used to initiate boron neutron capture was generated from a radioactive isotope of uranium, Uranium-235, licensed to the MIT reactor by the Nuclear Regulatory Commission.

33. In all the boron neutron capture therapy trials at MIT, the target for the neutron beam has always been boron-10 atoms that had been injected into patients in boron bearing compounds that will pass the brain's blood barrier. In later trials, the patients have had suffered from both glioblastoma multiforme and melanoma, that had metastasized to the brain.

34. When boron-10 nuclei are exposed to a neutron beam, they have a high affinity to absorb neutrons. When this absorption occurs an isotope of boron, boron-11, is created. Boron-11, however, after absorbing a neutron becomes energized and, therefore, unstable.

---

[1] This is the primary mechanism for boron neutron capture therapy.

[2] Emission of an electron from the nucleus.

[3] Emission of a positively charged electron that is immediately destroyed when it contacts a negative electron.

[4] Ionization.

35. This instability results in the spontaneous transformation of the Boron-11 nuclei into two new elements: helium (the alpha-particle) and lithium-7.

36. In 93% of the reactions, the transformation of boron-11 into helium and lithium also results in the creation of a low energy gamma ray (x-ray).

37. In all cases of the reaction, there is additional kinetic energy created that makes the lithium atom and the alpha particle recoil and move in opposite directions to conserve momentum.

38. Neither of these two particles have any electrons so they are ionized. Because they are heavy charged particles they only travel a short distance measured in millionths of an inch within the human body before they gain electrons and lose their kinetic energy.

39. In particular, it is generally known and accepted in the scientific community that alpha particles within the human body travel only four millions of an inch or approximately the diameter of one human cell. The alpha particles however do not have a pair of electrons to match the number of protons in the nucleus. As a result, in traveling within the body, they breakdown biochemical bonds by stripping and capturing electrons from these compounds. This of course causes cell damage and cell death which is the objective of boron neutron capture therapy since it is intended to be applied primarily to cancer cells.

40. The neutron beam produced by the MIT reactor is caused by the radioactive properties of the nuclear source material that the MIT reactor is licensed to hold and use originally by the Atomic Energy Commission and subsequently by the Nuclear Regulatory Commission.

41. It is my considered opinion based upon a reasonable degree of scientific certainty that the interaction of neutrons with boron-10 contained within cellular structures will cause localized damage via the generation of highly ionized particles from these interactions. The ionizing radiations produced from neutron interactions with boron-10 are the direct result of neutrons produced from the source material contained within the reactor.

SIGNED UNDER THE PAINS AND PENALTIES OF PERJURY THIS 3 DAY OF APRIL 2001.

[signature]

JOHN BERNARD, PH. D.

JOHN A. BERNARD, Ph.D., CHP, P.E.

Nuclear Reactor Laboratory
Massachusetts Institute of Technology
138 Albany Street
Cambridge, MA 02139
(617) 253-4202
(617) 253-7300 (FAX)
jbernard@mit.edu

Current Position:

- Director of the MIT Nuclear Reactor Laboratory, Director of Reactor Operations of the 5-MWt MIT Research Reactor, and
- Principal Research Engineer responsible for theoretical and experimental research as well as management of MIT program on the closed-loop, digital operation of nuclear reactors.

Interests:

- Closed-Loop Digital Control of Nuclear Reactors; Use of Nuclear Energy for the Exploration of Space; Artificial Intelligence Applications to Nuclear Reactors; Nuclear Medicine, particularly Neutron Capture Therapy; Health Physics; Radiation Biology; Operator Training; Reactor Operations; Energy Planning; and the Interaction of Technology and Law.

Education:

Massachusetts Institute of Technology

- Ph.D. in Nuclear Engineering for thesis entitled, "Development and Experimental Demonstration of Digital Closed-Loop Control Strategies for Nuclear Reactors," June 1984. (Minor in Urban Studies)
- Degrees of Nuclear Engineer and Master of Science in Nuclear Engineering for thesis entitled, "MITR-II Fuel Management, Core Depletion and Analysis: Codes Developed for the Diffusion Theory Program CITATION," June 1979.

United States Navy Nuclear Propulsion Program

- Naval Nuclear Power Training Unit, Schenectady (West Milton), New York, August 1971. Qualified for supervision, operation, and maintenance of a Naval Nuclear Propulsion Plant. Qualified as Engineering Officer of the Watch on the U.S. Navy's DIG pressurized water reactor. This was the senior watch station.
- Naval Nuclear Power School, Bainbridge, Maryland. Courses completed Jan. 1971.

Yale University

- Bachelor of Science in Engineering and Applied Science, June 1970.
- Commissioned as an Ensign, USNR, June 1970.

Qualifications:

- Certified Health Physicist, American Board of Health Physics. (11/98 - present)
- Licensed Professional Engineer (Nuclear), Commonwealth of Massachusetts.

Professional Experience:

Massachusetts Institute of Technology

Director, MIT Nuclear Reactor Laboratory. Responsible for scientific direction and management of the laboratory (6/99 – present).

- Chairman, National Organization of Test, Research, and Training Reactors. (10/97 - 10/98)
- Interim Director, MIT Nuclear Reactor Laboratory. Responsible for scientific direction and management of the laboratory. (10/96 - present)
- Chairman, National Organization of Test, Research, and Training Reactors. (10/90 - 10/91)
- Principal Research Engineer, MIT Department of Nuclear Engineering. (7/90 - present)
- Member of Executive Committee of National Organization of Test, Research, and Training Reactors. (10/89 - present)
- Director of Reactor Operations, MIT Research Reactor. Responsible for all aspects of the licensing and operation of the MIT Nuclear Research Reactor. This is the senior licensed position at MIT. (6/88 - present)
- Principal Research Engineer, MIT Nuclear Reactor Laboratory. (6/86 - present)
- Principal Investigator MIT Experiment/Design Group for the Application of Advanced Instrumentation and Control Techniques to Nuclear Reactors. Responsible for closed-loop control research, both theoretical and applied including determination of areas of study, experiment planning, safety evaluations, experiment implementation, and data evaluation. (6/80 - present)
- Superintendent, MIT Research Reactor. Responsible for operation of the MIT Reactor including routine 100 hour/week operation,

maintenance, test and calibrations, fuel management, radioactive material and waste shipments, revision of procedures, training, handling of NRC inspections, and preparation of emergency plans. Division consisted of ten licensed operators and three technicians. (8/79 - 6/88)

- Member of MIT Reactor Safeguards Committee. (8/79 - present)
- Senior Shift Supervisor on the MIT Research Reactor. Responsible for reactor startups and shutdowns, Q/A audits, sample and experiment safety evaluations, and fuel management calculations using the code CITATION. (6/76 - 8/79)
- Secretary to MIT Reactor Safeguards Committee (6/76 - 11/91) and (11/92 - 4/98)
- Reactor Operator on the MIT Research Reactor. Participated in initial core loading and spent fuel shipments. (3/75 - 6/76)

American Nuclear Society

- Member, Executive Committee of American Nuclear Society Operations and Power Division (6/00 – 6/03).
- Member, Board of Directors (6/99 – 6/00).
- Member, President's Task Force Infrastructure I (11/97 – 6/98).
- Chairman, American Nuclear Society Isotopes and Radiation Division. (6/97 - 6/98)
- Member, Executive Committee of American Nuclear Society Biology and Medicine Division. (6/96 – 6/99)
- Treasurer, American Nuclear Society Isotopes and Radiation Division. (6/95 - 6/96)
- Member, Book Publishing Committee of American Nuclear Society. (6/94 - present)
- Member, Executive Committee of American Nuclear Society Isotopes and Radiation Division. (6/94 - 6/99)
- Head, American Nuclear Society Isotopes and Radiation Division's Subcommittee on Research Reactors. (11/91 - present)

United States Navy

- Principal Assistant to the Department Head of the Reactor Department, the U.S.S. ENTERPRISE (CVA(N)-65). (9/73 - 6/74)

- Received meritorious promotion to Lieutenant for analysis of a corrosion-induced malfunction of a propulsion plant component and for supervision of the radiological aspects of several major plant repairs. (8/73)

- Assumed duties as Reactor Laboratory Division Officer. Responsible for maintaining proper chemical control of all primary and secondary plant water, radiological controls, and health physics. Division consisted of 25-30 men with an annual budget of $50,000 - $80,000, exclusive of salaries. (2/72 - 6/74)

- Qualified as Propulsion Plant Watch Officer on U.S.S. ENTERPRISE's Nuclear Propulsion Plant. This was the senior watch station. Experience obtained while serving on board U.S.S. ENTERPRISE (CVA(N)-65) included startup of nuclear reactors and associated steam plants from cold-iron to operating, reactor shutdowns, hydrostatic testing, inspection and repair of various primary system components including eddy-current testing of steam generator tubing, packaging and shipment of radioactive materials (liquid and solid), and writing specifications. (2/72 - 6/74)

- Reported aboard U.S.S. ENTERPRISE (CVA(N)-65) in Oct. 1971.

- Promoted to Lieutenant (jg) in Aug. 1971.

Teaching Experience:

- Professor for MIT Department of Nuclear Engineering's Course 22.581, "Introduction to Health Physics." (1998 – present)

- Organizer and lecturer for MIT Department of Nuclear Engineering's Course 22.921, "Reactor Dynamics and Control." (1996 - present)

- Organizer and lecturer for special problems in areas of engineering fundamentals, health physics, and radiation detection for students in the MIT Department of Nuclear Engineering's Radiation Science and Technology option. (1994 - present)

- Lecturer for MIT Dept. of Nuclear Engineering's course "Reactor Technology Executive Program" conducted for the Institute for Nuclear Power Operations. (1993 - present)

- Lecturer for MIT Dept. of Nuclear Engineering's course 22.58 on Health Physics. (1983 - 1990)

- Established several non-credit and one credit mini-course during MIT's Independent Activities Program. Topics include reactor dynamics, closed-loop reactor control, MITR-II fuel management. Lecturer for these courses. (1980 - 1995)

- Coordinator of training program under which thirty-four individuals have received reactor operator licenses and forty individuals have received senior reactor operator licenses on the MIT Research Reactor. (1979 - 1997)

Societies:

- American Nuclear Society (Fellow)
- Institute of Electrical and Electronics Engineers (Senior Member)
- Sigma Xi, the Scientific Research Society (Full Member)

Honors:

- U.S. and Vietnam Defense Medals
- Meritorious and Presidential Unit Citations
- Navy Achievement Medal
- "Best Paper Award for Reactor Safety" at 1986 ANS Topical Meeting on Reactor Physics and Safety
- "Best Presentation Award" at 1987 American Control Conference
- 1989 American Nuclear Society Young Member Engineering Achievement Award
- Elected Fellow of the American Nuclear Society, for *"the theoretical development and experimental demonstration of generic methods for the closed-loop digital control of both terrestrial and spacecraft nuclear reactors, including the reactivity constraint approach and period-generated control, as well as promotion of the understanding and use of expert systems technology within the nuclear industry,"* Oct. 1992.
- Alpha Nu Sigma 1998-1999 Outstanding Teacher Award (Massachusetts Beta Chapter (MIT) of National Honor Society for Nuclear Science and Engineering)

Patents:

- Apparatus and Method for Closed-Loop Control of Reactor Power: Standard Dynamic Period Equation (No. 4,637,911)

- Apparatus and Method for Closed-Loop Control of Reactor Power: Alternate Dynamic Period Equation (No. 4,710,341)
- Apparatus and Method for Closed-Loop Control of Reactor Power in Minimum Time (No. 4,781,881)
- Indirect Labeling Method for Post-Separation of Chemical Compounds (No. 5,071,775)
- Apparatus and Method for Closed-Loop Control of Reactor Power (No. 4,710,341 – Canada)

Publications of John A. Bernard

A. Books and Major Reports

1. Bernard, J.A. and D.D. Lanning, Fault-Tolerant Systems Approach Toward Closed-Loop Digital Control of Nuclear Power Reactors, CPE-8317878, National Science Foundation, Washington, D.C., Jan. 1988.

2. Bernard, J.A., "Applications of Artificial Intelligence to Reactor and Plant Control," in Artificial Intelligence Applications in the Nuclear Industry, Majumdar, D., Ed., DOE/ID-10191, Oct. 1988, pp 6-1 - 6-11.

3. Bernard, J.A., Formulation and Experimental Evaluation of Closed-Form Control Laws for the Rapid Maneuvering of Reactor Neutronic Power, Report No. MITNRL-030, Massachusetts Institute of Technology, Cambridge, MA, Sept. 1989.

4. Bernard, J.A. and T. Washio, Expert Systems Applications Within the Nuclear Industry, American Nuclear Society, La Grange Park, IL, Oct. 1989.

5. Bernard, J.A., Startup and Control of Nuclear Reactors Characterized by Space-Independent Kinetics, Report No. MITNRL-039, Massachusetts Institute of Technology, Cambridge, MA, May 1990.

6. Harling, O.K., Bernard, J.A., and R.G. Zamenhof, (Eds.), Neutron Beam Design, Development, and Performance for Neutron Capture Therapy, Plenum Press, New York, NY, September 1990.

7. Bernard, J.A., Henry, A.F., Lanning, D.D., and J.E. Meyer, Closed-Loop Digital Control of Nuclear Reactors Characterized by Spatial Dynamics, Report No. MITNRL-041, Massachusetts Institute of Technology, Cambridge, MA, Mar. 1991.

8. Bernard, J.A., Henry, A.F., Lanning, D.D., and J.E. Meyer, Studies on the Closed-Loop Digital Control of Multi-Modular Reactors Report No. MITNRL-049, Massachusetts Institute of Technology, Cambridge, MA, Nov. 1992.

9. Bernard, J.A., "Light Water Reactor Control Systems," in Encyclopedia of Electrical and Electronics Engineering, J. Webster, Ed., John Wiley & Sons, Inc., New York, NY, Vol. 11, pp 357-376, March 1999.

10. Bernard, J.A. and L.W. Hu, Safety Analysis Report for the MIT Research Reactor (MITR-III), Massachusetts Institute of Technology, Cambridge, MA, July 1999.

11. Bernard, J.A. and L.W. Hu, Technical Specifications for the MIT Research Reactor (MITR-III), Massachusetts Institute of Technology, Cambridge, MA, July 1999.

B. Journal and Conference Publications

1. Bernard, J.A., Lanning, D.D., and L. Clark, Jr., "Use of Element Rotation/Inversion to Increase MITR-II Fuel Depletion," Transactions of the American Nuclear Society, Vol. 38, Suppl. 1, Aug. 1981, pp 17-18.

2. Clark, L. Jr., Bernard, J.A., and E. Karaian, "Fuel Cladding Failure at the MIT Research Reactor," Transactions of the American Nuclear Society, Vol. 38, Suppl. 1, Aug. 1981, pp 25-26.

3. Ray, A., Lanning, D.D., and J.A. Bernard, "Computer-Aided Feedback Control of Power in a Fission Reactor," Proceedings of the International Association of Science and Technology for Development (IASTED), Cambridge, MA, July 1982, pp 119-122.

4. Ray, A., Bernard, J.A., and D.D. Lanning, "Computer Control of Power in a Nuclear Reactor," IEEE Transactions on Nuclear Science, Vol. NS-30, No. 1, Feb. 1983, pp 820-824.

5. Ray, A., Bernard, J.A., and D.D. Lanning, "On-Line Signal Validation and Feedback Control in a Nuclear Reactor," Proceedings of the Fifth Power Plant Dynamics, Control & Testing Symposium, Knoxville, TN, March 1983, Paper No. 38.

6. Ray, A. and J.A. Bernard, "Digital Controller for a Nuclear Reactor," Proceedings of the American Control Conference, San Francisco, CA, Vol. 3, June 1983, pp 978-983.

7. Bernard, J.A., Ray, A., and D.D. Lanning, "Digital Computer Control of a Nuclear Reactor," Transactions of the American Nuclear Society, Vol. 44, Suppl. 1, Aug. 1983, pp 64-66.

8. Bernard, J.A., Kwok, K.S., Lanning, D.D., and L. Clark, Jr., "Calculational Procedures Used to Extend MITR-II Fuel Burnup," Transactions of the American Nuclear Society, Vol. 44, Suppl. 1, Aug. 1983, pp 14-15.

9. Bernard, J.A., Lanning, D.D., Kwok, K.S., and A. Ray, "Demonstration of Decision Analysis Techniques for Steady-State Reactor Control," Transactions of the American Nuclear Society, Vol. 45, Nov. 1983, pp 661-662.

10. Bernard, J.A. and A. Ray, "Experimental Evaluation of Digital Control Schemes for Nuclear Reactors," Proceedings of the 22nd IEEE Control and Decision Conference, San Antonio, TX, Dec. 1983, pp 744-751.

11. Bernard, J.A., Ray, A., and D.D. Lanning, "Digital Control of Power Transients in a Nuclear Reactor," IEEE Transactions on Nuclear Science, Vol. NS-31, No. 1, Feb. 1984, pp 701-705.

*12. Bernard, J.A., Ray, A., and D.D. Lanning, "Development and Demonstration of Digital Computer Control of Nuclear Reactors," International Symposium on the Use and Development of Low and Medium Flux Research Reactors, Published as a Supplement to Atomkernenergie-Kerntechnik, Vol. 44 (1984), pp 460-466.

*13. Menadier, P., Bernard, J.A., and A. Ray, "Circuitry Design for the Installation of a Direct Digital Computer Control System on the MIT Research Reactor," International Symposium on the Use and Development of Low and Medium Flux Research Reactors, Published as a Supplement to Atomkernenergie-Kerntechnik, Vol. 44 (1984), pp 529-535.

*14. Kwok, K.S., Bernard, J.A., and L. Clark, Jr., "Operator Training at the MIT Research Reactor," International Symposium on the Use and Development of Low and Medium Flux Research Reactors, Published as a Supplement to Atomkernenergie-Kerntechnik, Vol. 44 (1984), pp 1031-1037.

*15. Gehret, J.B., Bernard, J.A., and O.K. Harling, "Potential Utilization of Waste Heat from the MIT Research Reactor," International Symposium on the Use and Development of Low and Medium Flux Research Reactors, Published as a Supplement to Atomkernenergie-Kerntechnik, Vol. 44 (1984), pp 1061-1068.

16. Bernard, J.A. and D.D. Lanning, "Reactivity Constraints and the Automatic Control of Reactor Power," Transactions of the American Nuclear Society, Vol. 47, Nov. 1984, pp 394-396.

*17. Bernard, J.A., Lanning, D.D., and A. Ray, "Experimental Evaluation of Reactivity Constraints for the Closed-Loop Control of Reactor Power,"

<u>Proceedings of the NRC-EPRI Symposium on New Technologies in Nuclear Power Plant Instrumentation and Control</u>, Washington, D.C., Nov. 1984, pp 99-111. (Published by Instrument Society of America.)

18. Bernard, J.A., Lanning, D.D., and A. Ray, "Use of Reactivity Constraints for the Automatic Control of Reactor Power," <u>IEEE Transactions on Nuclear Science</u>, Vol. NS-32, No. 1, Feb. 1985, pp 1036-1040.

19. Kwok, K.S., Snapka, R.M., Bernard, J.A., Harling, O.K., and A. Varshavsky, "Detection of Unlabeled, Separated, Biological Molecules via Neutron Activation," <u>Transactions of the American Nuclear Society</u>, Vol. 49, June 1985, pp 157-158.

20. Bernard, J.A., Kwok, K.S., and D.D. Lanning, "Experimental Evaluation of 'Fuzzy' Logic in Closed-Loop Reactor Control," <u>Transactions of the American Nuclear Society</u>, Vol. 49, June 1985, pp 392-393.

21. Lanning, D.D., Bernard, J.A., Hopps, J.H., and A. Ray, "MITR-II: Integrated Fault-Tolerant Systems Implementation and Experiments," <u>Transactions of the American Nuclear Society</u>, Vol. 49, June 1985, pp 377-378.

22. Bernard, J.A., Ray, A., Kwok, K.S., and D.D. Lanning, "Design and Experimental Evaluation of a 'Fuzzy' System for the Control of Reactor Power," <u>Proceedings of the American Control Conference</u>, Boston, MA, Vol. 3, June 1985, pp 1466-1474.

23. Bernard, J.A., Kwok, K.S., Lanning, D.D., and L. Clark, Jr., "Effect of Radial Power Distribution on MITR-II Fuel Element and Control Blade Worth," <u>Transactions of the American Nuclear Society</u>, Vol. 49, Suppl. 2, Aug. 1985, pp 53-54.

24. Kwok, K.S., Fecych, W., Shull, C.G., and J.A. Bernard, "Design and Use of an MITR-II Beam Port Facility for Undergraduate Education," <u>Transactions of the American Nuclear Society</u>, Vol. 49, Suppl. 2, Aug. 1985, pp 35-36.

*25. Bernard, J.A., Lanning, D.D., and A. Ray, "The Nuclear Industry and Digital Control: An Unrealized Opportunity," <u>INTECH</u>, Vol. 32, No. 9, Sept. 1985, pp 61-64.

26. Bernard, J.A. and D.D. Lanning, "Experimental Evaluation of the Reactivity Constraint Approach for the Closed-Loop Control of Reactor Power Over a Range of Differential Reactivities," <u>Proceedings of the American Nuclear Society Inter-national Topical Meeting on Computer Applications for Nuclear Power Plant Operation and Control</u>, Pasco, WA, Sept. 1985, pp 486-495.

27. Zamenhof, R.G., Madoc-Jones, H., Harling, O.K., and J.A. Bernard, "A Clinical Trial of Neutron Capture Therapy for Brain Tumors at New England Medical

Center and the Massachusetts Institute of Technology," Proceedings of the U.S. Department of Energy Workshop on Neutron Capture Therapy, BNL-51994, Brookhaven, NY, Jan. 1986, pp 55-76.

28. Bernard, J.A. and D.D. Lanning, "Issues in the Closed-Loop Digital Control of Reactor Power: The MIT Experience," IEEE Transactions on Nuclear Science, Vol. NS-33, No. 1, Feb. 1986, pp 992-997.

29. Bernard, J.A., Kwok, K.S., Ornedo, R.S., Lanning, D.D., and J.H. Hopps, "The Application of Digital Technology to the Control of Reactor Power: A Review of the MIT Reactor Experiments," Proceedings of the Sixth Power Plant Dynamics, Control & Testing Symposium, Knoxville, TN, April 1986, Vol. 2, pp 44.01 - 44.24.

30. Bernard, J.A., "The Construction and Use of a Knowledge Base in the Real-Time Control of Research Reactor Power," Proceedings of the Sixth Power Plant Dynamics, Control & Testing Symposium, Knoxville, TN, April 1986, Vol. 2, pp 57.01 - 57.25.

31. Bernard, J.A., "The Behavior of Component Terms in the Dynamic Period Equation," Transactions of the American Nuclear Society, Vol. 52, June 1986, pp 490-492.

32. Polenta, H.P., Ray, A., Menadier, P.T., Lanning, D.D., and J.A. Bernard, "Implementation of a Fault Detection Procedure," Proceedings of the American Control Conference, Seattle, WA, Vol. 1, June 1986, pp 176-181.

33. Bernard, J.A., Henry, A.F., and D.D. Lanning, "The Design and Experimental Evaluation of a Closed-Loop Digital Controller Based on an Alternate Formulation of the Dynamic Period Equation," Proceedings of the American Nuclear Society Topical Meeting on Reactor Physics and Safety, Saratoga Springs, NY, Sept. 1986, pp 610-621.

34. Bernard, J.A., "Human Approach to Process Control and the Provision of Predictive Information," Transactions of the American Nuclear Society, Vol. 53, Nov. 1986, pp 139-140.

*35. Snapka, R.M., Kwok, K.S., Bernard, J.A., Harling, O.K., and A. Varshavsky, "Post-Separation Detection of Nucleic Acids and Proteins by Neutron Activation," Proceedings of the National Academy of Sciences, USA, Vol. 83, (Biochemistry), Dec. 1986, pp 8939-8942.

36. Bernard, J.A., Kwok, K.S., Lanning, D.D., Henry, A.F., and J.E. Meyer, "Application of the Reactivity Constraint Approach to the Transient Control of Spacecraft Reactors," Transactions of the Fourth Symposium on Space Nuclear Power Systems, CONF-870102-Summs., Albuquerque, NM, Jan. 1987, pp 219-224.

*37. Bernard, J.A., "An Experimental Comparison of Reactor Power Controllers Based on the Standard and Alternate Formulations of the Dynamic Period Equation," IEEE Transactions on Nuclear Science, Vol. NS-34, No. 1, Feb. 1987, pp 548-552.

38. Bernard, J.A., Ornedo, R.S., and D.D. Lanning, "Human Approach to Process Control and the Role of Digital Technology," Proceedings of the American Control Conference, Minneapolis, MN, Vol. 2, June 1987, pp 934-940.

39. Ornedo, R.S., Bernard, J.A., Lanning, D.D., and J.H. Hopps, "Design and Experimental Evaluation of an Automatically Reconfigurable Controller for Process Plants," Proceedings of the American Control Conference, Minneapolis, MN, Vol. 3, June 1987, pp 1662-1668.

40. Bernard, J.A., "Time-Optimal Control of Reactor Power," Proceedings of the American Nuclear Society International Topical Meeting on Artificial Intelligence and Other Innovative Computer Applications in the Nuclear Industry, Snowbird, UT, Sept. 1987, pp 461-470.

41. Bernard, J.A., "Structure of Controllers for the Direct Digital Control of Reactor Power: Licensing Implications," Proceedings of the American Nuclear Society International Topical Meeting on Artificial Intelligence and Other Innovative Computer Applications in the Nuclear Industry, Snowbird, UT, Sept. 1987, Plenum Press, New York, NY, pp 483-492, 1988.

42. Harling, O.K., Bernard, J.A., Zamenhof, R.G.A., and H. Madoc-Jones, "A Clinical Trial of Neutron Capture Therapy for Brain Tumors," Proceedings of the International Symposium on the Utilization of Multipurpose Research Reactors and Related International Co-operation, Grenoble, France, Oct. 1987, pp 413-425, International Atomic Energy Agency, Vienna, 1988.

43. Harling, O.K., Bernard, J.A., and M.J. Driscoll, "Compact In-Pile Loops for Dose and Corrosion Reduction Research, and Development of Closed Loop Digital Control of Reactor Power," Proceedings of the International Symposium on the Utilization of Multipurpose Research Reactors and Related International Co-operation, Grenoble, France, Oct. 1987, pp 126-129, International Atomic Energy Agency, Vienna, 1988.

44. Bernard, J.A., "Use of a Rule-Based System for Process Control," Proceedings of the International Conference on Industrial Electronics, Control, and Instrumentation, SPIE Vol. 857, Nov. 1987, pp 835-847.

45. Bernard, J.A., "Derivation of the Standard Dynamic Period Equation," Transactions of the American Nuclear Society, Vol. 55, Nov. 1987, pp 598-600.

46. Bernard, J.A., "The Relation of the Inhour and the Dynamic Period Equations," Transactions of the American Nuclear Society, Vol. 55, Nov. 1987, pp 69-71.

47. Bernard, J.A., Kwok, K.S., Menadier, P.T., Thome, F.V., and F.J. Wyant, "Experimental Evaluation of the MIT-SNL Period-Generated Minimum Time Control Laws for the Rapid Adjustment of Reactor Power," Transactions of the Fifth Symposium on Space Nuclear Power Systems, CONF-880122-Summs., Albuquerque, NM, Jan. 1988, pp 589-594.

*48. Bernard, J.A., "Evaluation of 'Period-Generated' Control Laws for the Time-Optimal Control of Reactor Power," IEEE Transactions on Nuclear Science, Vol. NS-35, No. 1, Feb. 1988, pp 888-893.

*49. Bernard, J.A., Henry, A.F., and D.D. Lanning, "Application of the 'Reactivity Constraint Approach' to Automatic Reactor Control," Nuclear Science and Engineering, Vol. 98, No. 2, Feb. 1988, pp 87-95.

50. Zamenhof, R.G.A., Madoc-Jones, H., Harling, O.K., and J.A. Bernard, "Clinical Considerations in the Use of Thermal and Epithermal Neutron Beams for Neutron Capture Therapy," Proceedings of a Workshop on Boron Neutron Capture Therapy, Brookhaven National Laboratory, New York, Feb. 1-2, 1988. (in Basic Life Sciences, Vol. 50: Clinical Aspects of Neutron Capture Therapy, Plenum Press, New York, 1989, pp 121-134.)

51. Harling, O.K., Clement, S.D., Choi, J.R., Bernard, J.A., and R.G. Zamenhof, "Neutron Beams for Neutron Capture Therapy at the MIT Research Reactor," Proceedings of the Third International Symposium on Neutron Capture Therapy, Bremen, FRG, May 31 - June 31, 1988 (Strahlentherapie und Onkologie, Vol. 165, No. 2/3, Feb./Mar. 1989, pp 90-92.)

52. Zamenhof, R.G., Madoc-Jones, H., Harling, O.K., and J.A. Bernard, "A Multidisciplinary Program Leading to a Clinical Trial of Neutron Capture Therapy at Tufts-New England Medical Center and Massachusetts Institute of Technology," Proceedings of the Third International Symposium on Neutron Capture Therapy, Bremen, FRG, May 31 - June 31, 1988 (Strahlentherapie und Onkologie, Vol. 165, No. 2/3, Feb./Mar. 1989, pp 254-257.)

53. Lau, S.H., Bernard, J.A., Kwok, K.S., and D.D. Lanning, "Experimental Evaluation of Predictive Information as an Operator Aid in the Control of Research Reactor Power," Proceedings of the American Control Conference, Atlanta, GA, Vol. 1, June 1988, pp 214-220.

54. Aviles, B.N., Bernard, J.A., and D.D. Lanning, "The Design and Experimental Evaluation of a Non-Linear State-Variable Feedback Controller for Nuclear Reactors," Proceedings of the American Control Conference, Atlanta, GA, Vol. 1, June 1988, pp 263-265.

55. Bernard, J.A., Kwok, K.S., Thome, F.V., and F.J. Wyant, "The MIT-SNL Experiments Concerning the Closed-Loop Digital Control of Reactor Power,"

Proceedings of the ANS International Reactor Physics Conference, Jackson Hole, WY, Vol. IV, Sept. 1988, pp 193-206.

*56. Polenta, H.P., Ray, A., and J.A. Bernard, "Microcomputer-Based Fault Detection Using Redundant Sensors," IEEE Transactions on Industry Applications, Vol. IA-24, No. 5, Sept./Oct. 1988, pp 905-912.

*57. Bernard, J.A., "Use of a Rule-Based System for Process Control," IEEE Control Systems Magazine, Vol. 8, No. 5, Oct. 1988, pp 3-13.

58. Washio, T. and J.A. Bernard, "Development and Experimental Demonstration of a Noise Reduction Technique for a Non-Linear Dynamic System," Transactions of the American Nuclear Society, Vol. 57, Oct.-Nov. 1988, pp 96-97.

59. Bernard, J.A., "Inverse Dynamics and the Hybrid Method of Reactivity Measurement," Transactions of the American Nuclear Society, Vol. 57, Oct.-Nov. 1988, pp 103-104.

60. Bernard, J.A. and T. Washio, "An Examination of Expert Systems Activities Within the Nuclear Industry," Transactions of the American Nuclear Society, Vol. 57, Oct.-Nov. 1988, pp 240-241.

61. Bernard, J.A., Kwok, K.S., and T. Washio, "Autonomous Control of Spacecraft Nuclear Reactors," Proceedings of the SPIE Conference: Space Station Automation IV, SPIE Vol. 1006, Nov. 1988, pp 28-45.

62. Bernard, J.A., Kwok, K.S., Washio, T., Wyant, F.J., and F.V. Thome, "The Automated Startup of Spacecraft Nuclear Reactors," Transactions of the Sixth Symposium on Space Nuclear Power Systems, CONF-890103-Summs., Albuquerque, NM, Jan. 1989, pp 466-469.

63. Washio, T. and J.A. Bernard, "Stability Considerations and Noise Reduction in the Implementation of the MIT-SNL Period-Generated Minimum Time Control Laws," Transactions of the Sixth Symposium on Space Nuclear Power Systems, CONF-890103-Summs., Albuquerque, NM, Jan. 1989, pp 476-479.

*64. Bernard, J.A., "The Measurement of Reactivity Using Algorithms Derived from the Dynamic Period Equation," IEEE Transactions on Nuclear Science, Vol. NS-36, No. 1, Feb. 1989, pp 1270-1275.

*65. Bernard, J.A., Kwok, K.S., Lanning, D.D., Henry, A.F., and J.E. Meyer, "Transient Control of Reactor Power Generation for Rapid Maneuvering," in Space Nuclear Power Systems 1987, El-Genk, M.S. and M.D. Hoover, Eds., Orbit Book Co., Malabar, FL, Feb. 1989, pp 299-309.

66. Bernard, J.A., "Progress Toward a Generic Methodology for the Closed-Loop Digital Control of Nuclear Reactor Power," Proceedings of the ANS/NIST

Conference "Fifty Years with Nuclear Fission", Behrens, J.W. and A.D. Carlson, Eds., American Nuclear Society, La Grange Park, IL, Apr. 1989, pp 262-273.

*67. Bernard, J.A., "Applications of Artificial Intelligence to Reactor and Plant Control," Nuclear Engineering and Design, Vol. 130, No. 2, Apr. 1989, pp 219-227.

68. Bernard J.A., "A Review of the MIT Experiments on the Closed-Loop Digital Control of Reactor Power: 1985-1988," Proceedings of the Seventh Power Plant Dynamics, Control & Testing Symposium, Knoxville, TN, May 15-17, 1989, Vol. 2, pp 48.01 - 48.23.

69. Tuddenham, R.S., Lau, S.H., Washio, T., Bernard, J.A., and D.D. Lanning, "Experimental Demonstration of Proportional-Integral-Derivative Feedback in the Closed-Loop Digital Control of Reactor Neutronic Power," Proceedings of the Seventh Power Plant Dynamics, Control & Testing Symposium, Knoxville, TN, May 15-17, 1989, Vol. 2, pp 72.01 - 72.16.

70. Bernard, J.A. and T. Washio, "The Utilization of Expert Systems Within the Nuclear Industry," Proceedings of the American Control Conference, Pittsburgh, PA, Vol. 1, June 1989, pp 373-378, and also in Proceedings of the EPRI Conference on Expert Systems Applications in the Electric Power Industry, June 5-8, 1989, Orlando, FL.

71. Bernard, J.A., Kwok, K.S., Wyant, F.J., and F.V. Thome, "Demonstration of the Reactivity Constraint Approach on SNL's Annular Core Research Reactor," Transactions of the American Nuclear Society, Vol. 59, Suppl. 1, Aug. 1989, pp 28-30.

72. Lau, S.H., Bernard, J.A., Kwok, K.S., and D.D. Lanning, "Experimental Evaluation of Predictive Displays as an Operator Aid," Transactions of the American Nuclear Society, Vol. 59, Suppl. 1, Aug. 1989, pp 33-35.

73. Harling, O.K., Bernard, J.A., Driscoll, M.J., Kohse, G.E,. and R.G. Ballinger, "Engineering Activities at the MIT Research Reactor in Support of Power Reactor Technology," Transactions of the American Nuclear Society, Vol. 59, Suppl. 1, Aug. 1989, pp 23-25.

74. Harling, O.K. and J.A. Bernard, "The Value and Cost of University Research Reactors," Transactions of the American Nuclear Society, Vol. 60, Nov. 1989, pp 252-253.

75. Lau, S.H., Washio, T., Kwok, K.S., Bernard, J.A., Lanning, D.D., and F.J. Wyant, "A Methodology for the Control of Core Average Temperature in Spacecraft Nuclear Reactors," Transactions of the Seventh Symposium on Space Nuclear Power Systems, CONF-900109, Albuquerque, NM, Jan. 1990, pp 956-961.

*76. Bernard, J.A., Kwok, K.S., Menadier, P.T., Thome, F.V., and F.J. Wyant, "Experimental Evaluation of the MIT-SNL Period-Generated Minimum Time Control Laws for the Rapid Adjustment of Reactor Power," in Space Nuclear Power Systems 1988, El-Genk, M.S. and M.D. Hoover, Eds., Orbit Book Co., Malabar, FL, Feb. 1990, pp 495-508.

77. Bernard, J.A., Harling, O.K., and S.J. Kerekes, "The Nuclear Medicine Program at the MIT Research Reactor," Transactions of the American Nuclear Society, Vol. 61, June 1990, pp 110-112.

78. Bernard, J.A. and F.J. Wyant, "Recent Experimental Results from the MIT-SNL Program on the Control of Reactor Neutronic Power," Transactions of the American Nuclear Society, Vol. 61, June 1990, pp 124-126.

79. Bernard, J.A., "A Comparison of Trajectory Control Techniques in Robotics and Reactor Neutronics," Transactions of the American Nuclear Society, Vol. 62, Nov. 1990, pp 19-20.

80. Bernard, J.A., "A Comparison of Proportional and Model-Based Control Techniques for Nuclear Reactors," Proceedings of the Eighth Symposium on Space Nuclear Power Systems, CONF-910116, Albuquerque, NM, Jan. 1991, pp 693-701, American Institute of Physics, New York, 1991.

81. Bernard, J.A. and F.J. Wyant, "Experiments Illustrating the Importance of Automated Reasoning in Spacecraft Reactor Control," Proceedings of the Eighth Symposium on Space Nuclear Power Systems, CONF-910116, Albuquerque, NM, Jan. 1991, pp 1145-1195, American Institute of Physics, New York, 1991, and also in Proceedings of the American Control Conference, Boston, MA, Vol. 2, June 1991, pp 1096-1101.

*82. Bernard, J.A., "Demonstration of Feedback Using the MIT-SNL Minimum Time Control Laws for the Rapid Maneuvering of Reactor Power," IEEE Transactions on Nuclear Science, Vol. NS-38, No. 2, Apr. 1991, pp 838-844.

*83. Bernard, J.A., "Power Cutbacks as an Alternative to Scrams: An Application of the MIT-SNL Period-Generated Minimum Time Control Laws," IEEE Transactions on Nuclear Science, Vol. NS-38, No. 2, Apr. 1991, pp 516-524.

84. Bernard, J.A., "Application of the 'Variable Structure' Concept to the Control of Reactor Neutronic Power," Proceedings of the ANS International Topical Meeting on Advances in Mathematics, Computations, and Reactor Physics, Vol. 5, Apr. 1991, pp 24.1 (1-1 - 1-13).

85. Aviles, B.N., Lanning, D.D., and J.A. Bernard, "Supervisory Constraints for the Control of Neutronic and Thermal Power in a Pressurized Water Reactor (PWR)," Proceedings of the ANS International Topical Meeting on Advances in Mathematics, Computations, and Reactor Physics, Pittsburgh, PA, Vol. 5, Apr. 1991, pp 24.1 (2-1 - 2-13).

86. Bernard, J.A., "Period-Generated Control for Trajectory Tracking," Proceedings of the American Control Conference, Boston, MA, Vol. 3, June 1991, pp 3036-3037.

87. Lau, S.H., Bernard, J.A., and D.D. Lanning, "Experimental Evaluation of Feed-forward Control for the Trajectory Tracking of Power in Nuclear Reactors," Proceedings of the 26th Intersociety Energy Conversion Engineering Conference (IECEC), Boston, MA, Vol. 5, Aug. 1991, pp 13-19.

88. Kwok, K.S., Bernard, J.A., and D.D. Lanning, "Design, Assembly, and Initial Use of a Digital System for the Closed-Loop Control of a Nuclear Research Reactor," Proceedings of the 26th Intersociety Energy Conversion Engineering Conference (IECEC), Boston, MA, Vol. 5, Aug. 1991, pp 7-12.

89. Bernard, J.A. Lau, S.H., Kwok, K.S., Kim, K.K., and D.D. Lanning "Design, Installation, and Initial Use of a Smart Operator Aid," Proceedings of the Conference on Expert System Applications for the Electric Power Industry, Boston, MA, Sept. 9-11, 1991.

90. Lau, S.H., Bernard, J.A., and D.D. Lanning, "Experimental Comparison of Control Techniques for the Trajectory Tracking of Reactor Neutronic Power," Conference Proceedings of the IEEE Nuclear Science Symposium, Nov. 5-9, 1991, Santa Fe, NM.

91. Bernard, J.A., "Trajectory Tracking of Reactor Neutronic Power," Transactions of the American Nuclear Society, Vol. 64, Nov. 1991, pp 255-256.

92. Bernard, J.A., "Use of University Research Reactors to Teach Control Engineering," Transactions of the American Nuclear Society, Vol. 64, Nov. 1991, pp 258-259.

93. Kwok, K.S., Bernard, J.A., and D.D. Lanning, "Experimental Demonstration of Automated Reactor Startup with On-Line Reactivity Estimation," Proceedings of the Ninth Symposium on Space Nuclear Power Systems, CONF-920104, Albuquerque, NM, Jan. 1992, pp 562-571, AIP-246, American Institute of Physics, New York, 1992.

94. Bernard, J.A., "Period-Generated Control: A Space-Spinoff Technology," Proceedings of the Ninth Symposium on Space Nuclear Power Systems, CONF-920104, Albuquerque, NM, Jan. 1992, pp 583-593, AIP-246, American Institute of Physics, New York, 1992.

95. Bernard, J.A., Aviles, B.N., and D.D. Lanning, "Digital Control of Nuclear Reactors – Lessons Learned," Proceedings of the EPRI Conference on Advanced Digital Computers, Control, and Automation Technologies for Power Plants, San Diego, CA, Feb. 5-7, 1992.

96. Kwok, K.S., Bernard, J.A., and D.D. Lanning, "Derivation and Experimental Demonstration of the Perturbed Reactivity Method for the Determination of Subcriticality," Proceedings of the ANS Topical Meeting on Advances in Reactor Physics, Charleston, SC, Mar. 1992, pp 1-391 - 1-402.

97. Aviles, B.N., Lanning, D.D., and J.A. Bernard, "Design of a Multi-Tiered, Digital Controller for the Supervisory, Global, and Local Control of a Pressurized Water Reactor," Proceedings of the ANS Topical Meeting on Advances in Reactor Physics, Charleston, SC, Mar. 1992, pp 2-117 - 2-128.

98. Bernard, J.A., "Issues Regarding the Design and Acceptance of Intelligent Support Systems for Reactor Operators," Proceedings of the 2nd International Forum on Expert Systems and Computer Simulation in Energy Engineering, Erlangen, Germany, Mar. 17-20, 1992, pp 15-L-1 - 15-L-9.

*99. Bernard, J.A. and F.J. Wyant, "Experiments Illustrating the Importance of Automated Reasoning," IEEE Control Systems Magazine, Vol. 12, No. 2, Apr. 1992, pp 84-92.

*100. Bernard, J.A. and D.D. Lanning, "Considerations in the Design and Implementation of Control Laws for the Digital Operation of Research Reactors," Nuclear Science and Engineering, Vol. 110, No. 4, Apr. 1992, pp 425-444.

101. Bernard, J.A., "Experiments Demonstrating the Efficacy of Period-Generated Control for the Trajectory Tracking of Reactor Neutronic Power," Proceedings of the Eighth Power Plant Dynamics, Control & Testing Symposium, Knoxville, TN, May 27-29, 1992, Vol. 1, pp 29.01 - 29.14.

102. Bernard, J.A., "The Design of Intelligent Support Systems for Nuclear Reactor Operators," Transactions of the American Nuclear Society, Vol. 65, June 1992, pp 103-104.

*103. Bernard, J.A., "Non-Linear Control of Neutronic Power in Reactors Described by Space-Independent Kinetics," International Journal Control – Theory and Advanced Technology (C-TAT), Vol. 8, No. 3, Sept. 1992, pp 495-511.

*104. Bernard, J.A., "Issues Regarding the Design and Acceptance of Intelligent Support Systems for Reactor Operators," IEEE Transactions on Nuclear Science, Vol. NS-39, No. 5, Oct. 1992, pp 1549-1558.

105. Bernard, J.A., "Observations on the Development of Expert Systems for Nuclear Plants," Transactions of the American Nuclear Society, Vol. 66, Nov. 1992, pp 103-104.

106. Bernard, J.A., "Issues in the Management and Regulation of Non-Power Reactors," Transactions of the American Nuclear Society, Vol. 66, Nov. 1992, p 133.

*107. Bernard, J.A., Kwok, K.S., Washio, T., Wyant, F.J., and F.V. Thome, "Experimental Demonstration of the MIT-SNL Period-Generated Minimum Time Control Laws for Rapid Increases of Reactor Power from Subcritical Conditions," in Space Nuclear Power Systems 1989, El-Genk, M.S. and M.D. Hoover, Eds., Orbit Book Co., Malabar, FL, 1992, pp 381-392.

*108. Washio, T. and J.A. Bernard, "Stability Considerations Concerning the Implementation of the MIT-SNL Period-Generated Minimum Time Control Laws," in Space Nuclear Power Systems 1989, El-Genk, M.S. and M.D. Hoover, Eds., Orbit Book Co., Malabar, FL, 1992, pp 393-404.

109. Polenta, H.P., Bernard, J.A., and A. Ray, "Fault Detection System for Argentine Research Reactor Instrumentation," Proceedings of the Tenth Symposium on Space Nuclear Power and Propulsion, CONF-930103, Albuquerque, NM, Jan. 1993, pp 1275-1282, AIP-271, American Institute of Physics, New York, 1993.

110. Kim, K.K., Bernard, J.A., Meyer, J.E., and D.D. Lanning, "Digital Control of Power and Temperature in a PWR-Type Multi-Modular Reactor," Proceedings of the ANS Topical Meeting on Nuclear Plant Instrumentation, Control, and Man-Machine Interface Technologies, Oak Ridge, TN, Apr. 18-21, 1993, pp 599-697.

111. Bernard, J.A., "Challenges in the Application of Expert Systems to Nuclear Plant Instrumentation and Control," Proceedings of the ANS Topical Meeting on Nuclear Plant Instrumentation, Control, and Man-Machine Interface Technologies, Oak Ridge, TN, Apr. 18-21, 1993, pp 169-176.

112. Kim, K.K., Meyer, J.E., Lanning, D.D., and J.A. Bernard, "Design and Evaluation of Model-Based Compensators for the Control of Steam Generator Level," Proceedings of the American Control Conference, San Francisco, CA, Vol. 2, June 1993, pp 2055-2060.

113. Bernard, J.A., "License Amendment for Neutron Capture Therapy at the MIT Research Reactor," Transactions of the American Nuclear Society, Vol. 69, Nov. 1993, pp 161-162.

114. Harling, O.K., Kohse, G.E., Cabello, E.C., and J.A. Bernard, "Recent Results from the MIT In-Core Experiments on Coolant Chemistry," Transactions of the American Nuclear Society, Vol. 69, Nov. 1993, pp 162-163

115. Zamenhof, R.G., Wazer, D.E., Bernard, J.A., Harling, O.K., DiPetrillo, T.A., Madoc-Jones, H., Coderre, J.A., and A.G. Meek, "Federal and Institutional Approvals Necessary Prior to a U.S. Clinical Trial of Neutron Capture Therapy," Advances in Neutron Capture Therapy, Plenum Press, New York, 1993, pp 749-752.

116. Bernard, J.A., "An Acceleration-Based Reactor Control Law," Proceedings of the Eleventh Symposium on Space Nuclear Power and Propulsion, CONF-

940101, Albuquerque, NM, Jan. 1994, pp 497-503, American Institute of Physics, New York, 1994.

117. Bernard, J.A., "Derivation of an Acceleration-Based Control Law for Reactor Power," Transactions of the American Nuclear Society, Vol. 70, June 1994, pp 125-126.

118. Bernard, J.A., "Rationale for University Research Reactors," Transactions of the American Nuclear Society, Vol. 71, Nov. 1994, pp 160-161.

119. Bernard, J.A., "Suggestions on the Operation of PWR-Type Multi-Modular Reactor Plants," Transactions of the American Nuclear Society, Vol. 71, Nov. 1994, pp 366-367.

*120. Harling, O.K., Zamenhof, R.G., Solares, G.R., Yanch, J.C., Wazer, D.E., Rogus, R.D., Chabeuf, J.-M., Yam, S.C., Bernard, J.A., Cano, G., DiPetrillo, T., and H. Madoc-Jones, "Preparations for Phase I Clinical Trials of Boron Neutron Capture Therapy at the MIT Reactor and the New England Medical Center," Radiation Oncology Investigations, Vol. 2, No. 3, 1994, pp 109-118.

*121. Kim, K.K. and J.A. Bernard, "Considerations in the Control of Multimodular Reactor Plants," IEEE Transactions on Nuclear Science, Vol. T-NS-41, No. 6, Part II, Dec. 1994, pp 2686-2697.

122. Bernard, J.A., "A New Approach to the Investigation of Reactor Dynamics," Proceedings of the Ninth Power Plant Dynamics, Control & Testing Symposium, Knoxville, TN, May 24-26, 1995, Vol. 1, pp 5.01-5.10.

123. Bernard, J.A., "Procedures for Implementation of the MIT Program on Neutron Capture Therapy," Transactions of the American Nuclear Society, Vol. 72, Jun. 1995, pp 114-115.

124. Harling, O.K., Zamenhof, R.G., Bernard, J.A., Madoc-Jones, H., Solares, G.R., and C.-S. Yam, "Initiation of a Phase I Trial of Neutron Capture Therapy at the MIT Research Reactor," Transactions of the American Nuclear Society, Vol. 73, Oct. 29 - Nov. 2, 1995, pp 22-23.

125. Bernard, J.A., "State-Space Representation of the Reactor Dynamics Equations," Transactions of the American Nuclear Society, Vol. 73, Oct. 29 - Nov. 2, 1995, pp 301-302.

126. Bernard, J.A., "License Extension for the MIT Research Reactor," Transactions of the American Nuclear Society, Vol. 73, Oct. 29 - Nov. 2, 1995, pp 244-245.

127. Hu, L.-W., Meyer, J.E., and J.A. Bernard, "Forced Covection Mixing Transients in the MITR Core Tank," Transactions of the American Nuclear Society, Vol. 73, Oct. 29 - Nov. 2, 1995, pp 149-150.

128. Hu, L.-W., and J.A. Bernard, "Development of a Multi-Channel Analysis Code for MITR-III Safety Analysis," Transactions of the American Nuclear Society, Vol. 75, Nov. 10-14, 1996, pp 102-105.

129. Hu, L.-W., and J. A. Bernard, "Development and Benchmarking of a Thermal-Hydraulics Code for the MIT Nuclear Research Reactor," Proceedings of the ANS Joint International Conference on Mathematical Methods and Super-Computing for Nuclear Applications, Saratoga, NY, Oct. 5-7, 1997, pp 1117-1127.

130. Bernard, J.A., and L. W. Hu, "The Application of Reactor Physics Analysis Methods to the Interaction of Radiation with Tissue," Proceedings of the ANS Joint International Conference on Mathematical Methods and Super-Computing for Nuclear Applications, Saratoga, NY, Oct. 5-7, 1997, pp. 1329-1337.

131. Hu, L.-W., and J. A. Bernard, "Effect of Reactor Power on Bypass Channel Flow During Forced Convection," Transactions of the American Nuclear Society, Vol. 77, Nov. 16-20, 1997, pp 130-131.

132. Bernard, J. A., and L. W. Hu, "Analytical Approach to the Modeling of Radiation Effects in Tissue," Transactions of the American Nuclear Society, Vol. 77, Nov. 16-20, 1997, p 552.

133. Bernard, J.A., and L. W. Hu, "Dynamic Analysis of the Interaction of Radiation with Tissue," Conference Proceedings of the IEEE Nuclear Science Symposium, Nov. 10-14, 1997, Albuquerque, NM.

*134. Hu, L.-W., and J. A. Bernard, "Thermal-Hydraulic Analysis for the Upgraded MIT Nuclear Research Reactor," IEEE Transactions on Nuclear Science, Vol. 45, No. 3, Part I, June 1998, pp 1040-1044.

135. Hu, L.W., Bernard, J.A., Harling, O.K., Kohse, G.E., Ames, M., and Ilhan Olmez, "Current Activities at the MIT Research Reactor," Proceedings of the IGORR6 Meeting, Taejon, Republic of Korea, April 29-May 1, 1998.

136. Bernard, J.A., and L.W. Hu, "Significance of the Dynamic Response Equation for the Analysis of Radiation Effects on Tissue," Transactions of the American Nuclear Society, Vol. 78, June 7-11, 1998, pp. 8-10.

137. Hu, L.W., Bernard, J.A., and T.H. Newton, "Engineering Basis for the MIT Research Reactor Upgrade," Transactions of the American Nuclear Society, Vol. 78, June 7-11, 1998, p. 212.

138. Bernard, J.A., and L.W. Hu, "Contributions and Concerns of Women at the MIT Research Reactor," Transactions of the American Nuclear Society, Vol. 79, November 15-19, 1998, pp 37-38.

139. Hu, L.W., and J.A. Bernard, "Thermal-Hydraulic Analysis for the Licensing of the MITR Fission Converter," Transactions of the American Nuclear Society, Vol. 79, November 15-19, 1998, pp 96-97.

140. Hu, L.W., and J.A. Bernard, "Safety Features of the MIT Research Reactor's Fission Converter Facility," Transactions of the American Nuclear Society, Vol. 79, November 15-19, 1998, pp 97-98.

*141. Bernard, J.A., and L.W. Hu, "Dynamic Period Equation: Derivation, Relation to Inhour Equation, and Precursor Estimation," IEEE Transactions on Nuclear Science, Vol. 46, No. 3, Part I, June 1999, pp 433-437.

142. Hu, L.W., and J. A. Bernard, "Thermal-Hydraulic Criteria for the MIT Research Reactor Safety Limits Calculation," Transactions of the American Nuclear Society, Vol. 80, November 14-18, 1999, pp 114-115.

143. Li, Q., and J. A. Bernard, "Interaction of Period-Generated Control and the Reactivity Constraint Approach," Transactions of the American Nuclear Society, vol. 80, November 14-18, 1999, pp 115-116.

144. Bernard, J.A., and L.W. Hu, "University Research Reactors: Issues and Challenges," Conference Proceedings of the IEEE Nuclear Science Symposium, Nov. 8-14, 1998, Toronto, Canada and Nuclear Technology, Vol. 131, No. 3, September 2000, pp 379-384.

*Denotes refereed publication

Invited Lectures

1. "The Physics of Nuclear Reactor Operations and Safety" presented at the Physics Symposium on Nuclear Energy and Nuclear Reactors held in conjunction with the Annual Meeting of the New England Section of the American Association of Physics Teachers, 8 November 1986.

2. "TMI, Chernobyl, and the Future of Nuclear Power" presented at the Physics and Astronomy Colloquium at the University of Massachusetts at Amherst, Amherst, MA, 18 March 1987.

3. "Reactor Control Strategies" presented at the Workshop on Computerized Controls for Research Reactors sponsored by Directorate of Nuclear Surety, Department of the Air Force, Kirtland Air Force Base, New Mexico, 22 April 1987.

4. "Digital Control of Spacecraft Nuclear Reactors" presented at the Nuclear Engineering Department Seminar at the Pennsylvania State University, State College, PA, 27 March 1990.

5. "Nuclear Medicine" presented at the High School Science Teachers Program of "Science Education: Workshop 90" organized by the Education Outreach Committee, Institute for Space Nuclear Power Systems, Albuquerque, NM, 7 January 1991.

6. "Stellar Evolution" presented at the High School Science Teachers Program of "Science Education: Workshop 91" organized by the Education Outreach Committee, Institute for Space Nuclear Power Systems, Albuquerque, NM, 13 January 1992.

7. "Issues Regarding the Design and Acceptance of Intelligent Support Systems for Reactor Operators." Keynote Address to the 2nd International Forum on Expert Systems and Computer Simulation in Energy Engineering, Erlangen, Germany, 19 March 1992.

8. "Design, Installation, and Use of Digital Systems for Non-Power Reactors." Panel Discussion at the 1994 Winter Meeting of the American Nuclear Society, Washington, D.C., 13-17 November 1994.

9. "Neutron Capture Therapy at the MIT Research Reactor" presented at the Monthly Meeting of the Boston Chapter of the IEEE Nuclear Plasma Society, Cambridge, MA, 14 December 1994.

10. "Controller System to Aid Diagnostics," presented to the System Analysis Section of the Reactor Engineering Division of the Argonne National Laboratory, Argonne, IL, 29 November 1999.

11. "Digital Control of Nuclear Reactors: Theory and Experiments," Presentation to INER, Taiwan, September, 2000.

Professional Activities

A. Organizing Committees

1. International Symposium on the Use and Development of Low and Medium Flux Research Reactors, Cambridge, MA, Oct. 1983.

2. International Workshop on Neutron Beam Design, Development, and Performance for Neutron Capture Therapy, Cambridge, MA, March 1990.

3. Annual Meeting of the National Organization of Test, Research, and Training Reactor Managers (TRTR), Cambridge, MA, Oct. 1991.

4. Annual Meeting of the National Organization of Test, Research, and Training Reactor Managers (TRTR), Cambridge, MA, Dec. 1998.

B. Technical Program Committees

1. International Symposium on the Use and Development of Low and Medium Flux Research Reactors, Cambridge, MA, Oct. 1983.

2. 5th Symposium on Space Nuclear Power Systems, Albuquerque, NM, Jan. 1988.

3. 6th Symposium on Space Nuclear Power Systems, Albuquerque, NM, Jan. 1989.

4. American Nuclear Society Reactor Operations Division 1989 Biennial Meeting, Charlotte, NC, Aug. 1989.

5. 7th Symposium on Space Nuclear Power Systems, Albuquerque, NM, Jan. 1990.

6. International Workshop on Neutron Beam Design, Development, and Performance for Neutron Capture Therapy, Cambridge, MA, Mar. 1990.

7. 8th Symposium on Space Nuclear Power Systems, Albuquerque, NM, Jan. 1991.

8. AI 91 – Frontiers in Innovative Computing for the Nuclear Industry, Jackson Hole, WY, Sept. 1991.

9. Annual Meeting of the National Organization of Test, Research, and Training Reactor Managers (TRTR), Cambridge, MA, Oct. 1991.

10. 9th Symposium on Space Nuclear Power Systems, Albuquerque, NM, Jan. 1992.

11. 2nd International Forum on Expert Systems and Computer Simulations in Energy Engineering, Erlangen, Germany, Mar. 1992.

12. 16th Reactor Operations International Topical Meeting, Long Island, NY, Aug. 1993.

13. 2nd American Nuclear Society Topical Meeting on Nuclear Plant Instrumentation, Control and Human-Machine Interface Technologies, State College, PA, May 1996.

14. Annual Meeting of the National Organization of Test, Research, and Training Reactor Managers (TRTR), Cambridge, MA, Dec. 1998.

C. Technical Sessions Organized

1. "Control of Safety-Constrained Processes," at the 1985 American Control Conference, Boston, MA, June 19-21, 1985.

2. "Instrumentation and Control II," at the 5th Symposium on Space Nuclear Power Systems, Albuquerque, NM, Jan. 11-14, 1988.

3. "Reactor and Power System Control," at the 6th Symposium on Space Nuclear Power Systems, Albuquerque, NM, Jan. 8-12, 1989.

4. "Test, Research, and Training Reactor Utilization," at the American Nuclear Society's 14th Biennial Conference on Reactor Operating Experience – Plant Operations: The Human Element, Charlotte, NC, Aug. 6-9, 1989.

5. "Test, Research, and Training Reactor Upgrades," at the American Nuclear Society's 14th Biennial Conference on Reactor Operating Experience – Plant Operations: The Human Element, Charlotte, NC, Aug. 6-9, 1989.

6. "Reactor and Power System Control," at the 7th Symposium on Space Nuclear Power Systems, Albuquerque, NM, Jan. 7-10, 1990.

7. "Research Reactors – Applications in Nuclear Medicine," at the 1990 Annual Meeting of the American Nuclear Society, Nashville, TN, June 10-14, 1990.

8. "Artificial Intelligence in Space," at the 8th Symposium on Space Nuclear Power Systems, Albuquerque, NM, Jan. 6-10, 1991.

9. "Digital Control of Nuclear Reactors," at the 1991 Winter Meeting of the American Nuclear Society, San Francisco, CA, Nov. 10-14, 1991.

10. "Neutron Capture Therapy: Parts I and II," at the 1992 Annual Meeting of the American Nuclear Society, Boston, MA, June 7-12, 1992.

11. "Radiation Protection Issues at Non-Power Reactors," at the 1992 Winter Meeting of the American Nuclear Society, Chicago, IL, Nov. 15-20, 1992.

12. "New and Improved Experimental Facilities at Non-Power Reactors," at the 1992 Winter Meeting of the American Nuclear Society, Chicago, IL, Nov. 15-20, 1992.

13. "Research Programs at Non-Power Reactors," at the 1993 Annual Meeting of the American Nuclear Society, San Diego, CA, June 20-24, 1993.

14. "Societal Contributions of Non-Power Reactors," at the 1993 Winter Meeting of the American Nuclear Society, San Francisco, CA, Nov. 14-19, 1993.

15. "Recent Accomplishments at Non-Power Reactors," at the 1994 Annual Meeting of the American Nuclear Society, New Orleans, LA, June 19-24, 1994.

16. "Student Thesis Research at Non-Power Reactors," at the 1994 Winter Meeting of the American Nuclear Society, Washington, DC, November 13-17, 1994.

17. "Challenges to the Non-Power Reactor Community," at the 1994 Winter Meeting of the American Nuclear Society, Washington, DC, November 13-17, 1994.

18. "Update on Boron Neutron Capture Therapy," at the 1995 Winter Meeting of the American Nuclear Society, San Francisco, CA, October 29 - November 2, 1995.

19. "Student Thesis Research at Non-Power Reactors," at the 1995 Winter Meeting of the American Nuclear Society, San Francisco, CA, October 29 - November 2, 1995.

20. "Research Reactors: New Facilities and Techniques Update," at the 1996 Annual Meeting of the American Nuclear Society, Reno, NV, June 16-20, 1996.

21. "Engineering Applications in the Operation and Use of Non-Power Reactors," at the 1996 Winter Meeting of the American Nuclear Society, Washington, D.C., Nov. 10-14, 1996.

22. "Using Research Reactors for Medical Applications and Research," at the 1997 Winter Meeting of the American Nuclear Society, Albuquerque, NM, Nov. 16-20, 1997.

23. "Status of Boron Neutron Capture Therapy," at the 1999 Annual Meeting of the American Nuclear Society, Boston, MA, June 6-10, 1999.

24. "Nuclear and Related Analytical Techniques" at the 1999 Annual Meeting of the American Nuclear Society, Boston, MA, June 6-10, 1999.

D. Review Activities

1. Reviewer for IEEE Transactions on Nuclear Science (D. Mack/P. Dressendorfer, eds.), 1988 – present.

2. Reviewer for Nuclear Technology (W. Vogelsang/N. Tsoulfanidis, eds.), 1989 – present.

3. Reviewer for Nuclear Science and Engineering (D. Cacuci, ed.), 1991 – present.

4. Member, Manuel Lujan Jr. Student Paper Award Committee for the Symposia on Space Nuclear Power Systems, 1988-1991.

E. Consulting

1. Science Applications International Corporation (SAIC)

   – EPRI/NRC Verification and Validation Study on Expert Systems. (1990-1991)

2. International Atomic Energy Agency (IAEA)

   – Review of Standards in the Use of Digital I & C Systems for Non-Power Reactors. (1995)

3. General Atomics (GA)

   – Operational Considerations Regarding a Heavy-Water Reflected Research Reactor. (1995)

   - Design of a Heavy-Water Reflected Research Reactor. (1997-1998)

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

WILLIAM H. SWEET, M.D., and MASSACHUSETTS INSTITUTE OF TECHNOLOGY Plaintiffs	)	
v.	)	Nos. 00-274C, 00-292C (Judge Firestone)
THE UNITED STATES Defendant	)	

AFFIDAVIT OF CAROLYN DULONG, MIT KEEPER OF THE RECORDS

I, Carolyn Dulong, aver:

I am employed by the Massachusetts Institute of Technology ("MIT"). I made a diligent search of the books and records of MIT for Indemnity Agreement No. E-39 by and between MIT and the Nuclear Regulatory Commission, formerly the Atomic Energy Commission and any and all amendments thereto. The Indemnity Agreement and Amendments numbered 1 through 12 attached hereto were located with the exception of Amendment No. 8 which could not be found. I contacted the Nuclear Regulatory Commission which forwarded to me Amendment No. 8. The attached Indemnity Agreement No E-39 and corresponding amendments are records of MIT kept in the usual and ordinary course of operations of MIT.

Signed under the pains and penalties of perjury this 5th day of April, 2001

Carolyn R Dulong 4-5-01
Carolyn Dulong

UNITED STATES
ATOMIC ENERGY COMMISSION
WASHINGTON 25, D.C.

Indemnity
Agreement E-39
No.

This indemnity agreement No. E-39 is entered into by and between Massachusetts Institute of Technology (hereinafter referred to as the "licensee") and the United States Atomic Energy Commission (hereinafter referred to as the "Commission") pursuant to subsection 170k of the Atomic Energy Act of 1954, as amended (hereinafter referred to as "the Act").

ARTICLE I

As used in this agreement,

1. "Nuclear reactor", "byproduct material", "person", "source material", and "special nuclear material" shall have the meanings given them in the Atomic Energy Act of 1954, as amended, and the regulations issued by the Commission.

2(a) "Nuclear incident" means any occurrence or series of occurrences at the location or in the course of transportation causing bodily injury, sickness, disease, or death, or loss of or damage to property, or loss of use of property, arising out of or resulting from the radioactive, toxic, explosive, or other hazardous properties of the radioactive material.

(b) Any occurrence or series of occurrences causing bodily injury, sickness, disease or death, or loss of or damage to property, or loss of use of property, arising out of or resulting from the radioactive, toxic, explosive, or other hazardous properties of

i. The radioactive material discharged or dispersed from the location over a period of days, weeks, months or longer and also arising out of such properties of other material defined as "the radioactive material" in any other agreement or agreements entered into by the Commission under subsection 170 c or k of the Act and so discharged or dispersed from "the location" as defined in any such other agreement; or

ii. The radioactive material in the course of transportation and also arising out of such properties of other material defined in any other agreement entered into by the Commission pursuant to subsection 170 c or k of the Act as "the radioactive material" and which is in the course of transportation

6

shall be deemed to be a common occurrence. A common occurrence shall be deemed to constitute a single nuclear incident.

3. "In the course of transportation" means in the course of transportation within the United States, including handling or temporary storage incidental thereto, of the radioactive material to the location or from the location provided that:

(a) With respect to transportation of the radioactive material to the location, such transportation is not by pre-determination to be interrupted by the removal of the material from the transporting conveyance for any purpose other than the continuation of such transportation to the location or temporary storage incidental thereto;

(b) The transportation of the radioactive material from the location shall be deemed to end when the radioactive material is removed from the transporting conveyance for any purpose other than the continuation of transportation or temporary storage incidental thereto;

(c) "In the course of transportation" as used in this agreement shall not include transportation of the radioactive material to the location if the material is also "in the course of transportation" from any other "location" as defined in any other agreement entered into by the Commission pursuant to subsection 170 c or k of the Act.

4. "Person indemnified" means the licensee and any other person who may be liable for public liability.

5. During the period 12:01 A.M., June 9, 1958 to 12:01 A.M., September 6, 1961, inclusive:

"Public liability" means any legal liability arising out of or resulting from a nuclear incident, except (1) claims under state or Federal Workmen's Compensation Acts of employees of persons indemnified who are employed (a) at the location or, if the nuclear incident occurs in the course of transportation of the radioactive material, on the transporting vehicle, and (b) in connection with the licensee's possession, use, or transfer of the radioactive material; and (2) claims arising out of an act of war.

From 12:01 A.M., September 6, 1961:

"Public liability" means any legal liability arising out of or resulting from a nuclear incident, except (1) claims under state or Federal Workmen's Compensation Acts of employees of persons indemnified who are employed (a) at the location or, if the nuclear incident occurs in the course of transportation of the radioactive material, on the transporting vehicle, and (b) in connection with the licensee's possession, use, or transfer of the radioactive material; (2) claims arising out of an act of war; and (3) claims for loss of, or damage to, or loss of use of (a) property which is located at the location and used in connection with the licensee's possession, use, or transfer of the radioactive material, and (b), if the nuclear incident occurs in the course of transportation of the radioactive material, the transporting vehicle, containers used in such transportation, and the radioactive material.

6. "The location" means the location described in Item 3 of the Attachment hereto.

7. "The radioactive material" means source, special nuclear, and byproduct material which (1) is used or to be used in, or is irradiated or to be irradiated by, the nuclear reactor or reactors subject to the license or licenses designated in the Attachment hereto, or (2) is produced as the result of operation of said reactor(s).

8. "United States" when used in a geographical sense includes all Territories and possessions of the United States, the Canal Zone and Puerto Rico.

ARTICLE II

Any obligations of the licensee under subsection 53e(8) of the Act to indemnify the United States and the Commission from public liability shall not in the aggregate exceed $250,000 with respect to any nuclear incident.

ARTICLE III

1. The Commission undertakes and agrees to indemnify and hold harmless the licensee and other persons indemnified, as their interest may appear, from public liability.

2. With respect to damage caused by a nuclear incident to property of any person legally liable for the nuclear incident, the Commission agrees to pay to such person those sums which such person would have been obligated to pay if such property had belonged to another; provided, that the obligation of the Commission under this paragraph 2 does not apply with respect to:

(a) Property which is located at the location and used in connection with the licensee's possession, use, or transfer of the radioactive material;

(b) Property damage due to the neglect of the person indemnified to use all reasonable means to save and preserve the property after knowledge of a nuclear incident;

(c) If the nuclear incident occurs in the course of transportation of the radioactive material, the transporting vehicle and containers used in such transportation;

(d) The radioactive material.

3. The Commission agrees to indemnify and hold harmless the licensee and other persons indemnified, as their interest may appear, from the reasonable costs of investigating, settling and defending claims for public liability.

4. (a) The obligations of the Commission under this Article shall apply only with respect to such public liability, such damage to property of persons legally liable for the nuclear incident (other than such property described in the proviso to paragraph 2 of this Article) and such reasonable costs described in paragraph 3 of this Article as in the aggregate exceed $250,000.

(b) With respect to a common occurrence, the obligations of the Commission under this Article shall apply only with respect to such public liability, such damage to property of persons legally liable for the nuclear incident (other than such property described in the proviso to paragraph 2 of this Article) and to such reasonable costs described in paragraph 3 of this Article as in the aggregate exceed whichever of the following is lower: (1) the sum of the amounts of financial protection established under all applicable agreements; or (2) $60,000,000. As used in this paragraph, "applicable agreements" means each agreement entered into by the Commission pursuant to subsection 170c of the Act in which agreement the nuclear incident is defined as a "common occurrence."

5. The obligations of the Commission under this agreement shall apply only with respect to nuclear incidents occurring during the term of this agreement.

6. The obligations of the Commission under this and all other agreements and contracts to which the Commission is a party shall not in the aggregate exceed $500,000,000 with respect to any nuclear incident.

7. If the licensee is immune from public liability because it is a state agency, the Commission shall make payments under this agreement in the same manner and to the same extent as the Commission would be required to do if the licensee were not such a state agency.

8. The obligations of the Commission under this Article, except to the licensee for damage to property of the licensee, shall not be affected by any failure on the part of the licensee to fulfill its obligations under this agreement. Bankruptcy or insolvency of the licensee or any other person indemnified or of the estate of the licensee or any other person indemnified shall not relieve the Commission of any of its obligations hereunder.

ARTICLE IV

1. When the Commission determines that the United States will probably be required to make indemnity payments under the provisions of this agreement, the Commission shall have the right to collaborate with the licensee and other persons indemnified in the settlement and defense of any claim and shall have the right (a) to require the prior approval of the Commission for the settlement or payment of any claim or action asserted against the licensee or other person indemnified for public liability or damage to property of persons legally liable for the nuclear incident which claim or action the licensee or the Commission may be required to indemnify under this agreement; and (b) to appear through the Attorney General of the United States on behalf of the licensee or other person indemnified, take charge of such action and settle or defend any such action. If the settlement or defense of any such action or claim is undertaken by the Commission, the licensee shall furnish all reasonable assistance in effecting a settlement or asserting a defense.

2. Neither this agreement nor any interest therein nor claim thereunder may be assigned or transferred without the approval of the Commission.

ARTICLE V

The parties agree that they will enter into appropriate amendments of this agreement to the extent that such amendments are required pursuant to the Atomic Energy Act of 1954, as amended, or licenses, regulations or orders of the Commission.

ARTICLE VI

The licensee agrees to pay to the Commission such fees as are established by the Commission pursuant to regulations or orders of the Commission.

ARTICLE VII

The term of this agreement shall commence as of the date and time specified in Item 4 of the Attachment and shall terminate at the time of expiration of that license specified in Item 2 of the Attachment, which is the last to expire; provided that, except as may otherwise be provided in applicable regulations or orders of the Commission, the term of this

agreement shall not terminate until all the radioactive material has been removed from the location and transportation of the radioactive material from the location has ended as defined in subparagraph 3(b), Article I. Termination of the term of this agreement shall not affect any obligation of the licensee or any obligation of the Commission under this agreement with respect to any nuclear incident occurring during the term of this agreement.

UNITED STATES ATOMIC ENERGY COMMISSION

Indemnity Agreement No. E-39

ATTACHMENT

Item 1 - Licensee Massachusetts Institute of Technology

Address Cambridge 39, Massachusetts

Item 2 - License number or numbers

R-37

Item 3 - Location

The Reactor Building with stack and cooling towers including the area circumscribed by a chain link fence on the north and south sides of said building; a concrete wall and chain link fence on the east side of said building; and a line coinciding with the east wall of the Nuclear Engineering Building (Room NW12). Also, that portion of the Nuclear Engineering Building north of the partition extending from the southeast corner of the Transformer Vault (Room 123) to the southwest corner of the Spectrometer Set-up Room (Room 119); and, the fuel storage vault rooms identified as NW12-127, NW12-213 and NW12-313 and the connecting corridors and the elevator when nuclear fuels are being moved to and from the vaults and the areas first mentioned. The location is further depicted on the two prints, "Building NW12 and Reactor," dated May 1, 1964 and transmitted with the Institute's letter of May 7, 1964. Said prints are made part of this indemnity agreement by reference.

The above location is a portion of the facilities commonly known as 120 through 138 Albany Street, Cambridge, Massachusetts.

Item 4 - The indemnity agreement designated above, of which this Attachment is a part, is effective as of 12:01 A.M., on the 9th day of June, 1958 and supersedes the interim indemnity agreement between the licensee and the Atomic Energy Commission dated May 25, 1959.

FOR THE UNITED STATES ATOMIC ENERGY COMMISSION

By [signature]
Eber R. Price, Director
Division of State and Licensee Relations

For the MASSACHUSETTS INSTITUTE OF TECHNOLOGY
(Name of Licensee)

By [signature]
Paul V. Cusick COMPTROLLER

Dated at Bethesda, Maryland, the 13th
day of May, 1964.

AMENDMENT TO INDEMNITY AGREEMENT NO. E-39

AMENDMENT NO. 1

Effective January 1, 1966, Indemnity Agreement No. E-39, between Massachusetts Institute of Technology and the Atomic Energy Commission dated May 13, 1964, is hereby amended as follows:

Paragraph 4(b) of Article III is amended to read as follows:

(b) With respect to a common occurrence, the obligations of the Commission under this Article shall apply only with respect to such public liability, such damage to property of persons legally liable for the nuclear incident (other than such property described in the proviso to paragraph 2 of this Article) and to such reasonable costs described in paragraph 3 of this Article as in the aggregate exceed whichever of the following is lower: (1) the sum of the amounts of financial protection established under all applicable agreements; or (2) $74,000,000. As used in this Article, "applicable agreements" means each agreement entered into by the Commission pursuant to subsection 170c of the Act in which agreement the nuclear incident is defined as a "common occurrence."

Paragraph 6 of Article III is amended to read as follows:

6. The obligations of the Commission under this and all other agreements and contracts to which the Commission is a party shall not, with respect to any nuclear incident, in the aggregate exceed whichever of the following is the lower: (a) $500,000,000 or (b) with respect to a common occurrence, $560,000,000 less the sum of the amounts of financial protection established under all applicable agreements.

FOR THE UNITED STATES ATOMIC ENERGY COMMISSION

Eber R. Price, Director
Division of State and Licensee Relations

Accepted SEP 6 1966, 19

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

By Paul V. Cusick, Comptroller

UNITED STATES
ATOMIC ENERGY COMMISSION
WASHINGTON, D.C. 20545

AMENDMENT NO. 2 TO INDEMNITY AGREEMENT NO. E-39

Effective NOV 3 0 1968, Indemnity Agreement No. E-39, dated May 13, 1964, as amended, is hereby further amended in its entirety, and the following substituted therefor:

This Indemnity Agreement No. E-39 is entered into by and between the

Massachusetts Institute of Technology

(hereinafter referred to as the "licensee") and the United States Atomic Energy Commission (hereinafter referred to as the "Commission") pursuant to subsection 170k of the Atomic Energy Act of 1954, as amended (hereinafter referred to as "the Act").

ARTICLE I

As used in this agreement:

1. "Nuclear reactor," "byproduct material," "person," "source material," and "special nuclear material" shall have the meanings given them in the Atomic Energy Act of 1954, as amended, and the regulations issued by the Commission.

2.(a) "Nuclear incident" means any occurrence, including an extraordinary nuclear occurrence, or series of occurrences at the location or in the course of transportation causing bodily injury, sickness, disease, or death, or loss of or damage to property, or loss of use of property, arising out of or resulting from the radioactive, toxic, explosive, or other hazardous properties of the radioactive material.

(b) Any occurrence, including an extraordinary nuclear occurrence, or series of occurrences causing bodily injury, sickness, disease or death, or loss of or damage to property, or loss of use of property, arising out of or resulting from the radioactive, toxic, explosive, or other hazardous properties of

i. The radioactive material discharged or dispersed from the location over a period of days, weeks, months or longer and also arising out of such properties of other material

defined as "the radioactive material" in any other agreement or agreements entered into by the Commission under subsection 170c or k of the Act and so discharged or dispersed from "the location" as defined in any such other agreement; or

ii. The radioactive material in the course of transportation and also arising out of such properties of other material defined in any other agreement entered into by the Commission pursuant to subsection 170c or k of the Act as "the radioactive material" and which is in the course of transportation

shall be deemed to be a common occurrence. A common occurrence shall be deemed to constitute a single nuclear incident.

3. "Extraordinary nuclear occurrence" means an event which the Commission has determined to be an extraordinary nuclear occurrence as defined in the Atomic Energy Act of 1954, as amended.

4. "In the course of transportation" means in the course of transportation within the United States, including handling or temporary storage incidental thereto, of the radioactive material to the location or from the location provided that:

(a) With respect to transportation of the radioactive material to the location, such transportation is not by predetermination to be interrupted by the removal of the material from the transporting conveyance for any purpose other than the continuation of such transportation to the location or temporary storage incidental thereto;

(b) The transportation of the radioactive material from the location shall be deemed to end when the radioactive material is removed from the transporting conveyance for any purpose other than the continuation of transportation or temporary storage incidental thereto;

(c) "In the course of transportation" as used in this agreement shall not include transportation of the radioactive material to the location if the material is also "in the course of transportation" from any other "location" as defined in any other agreement entered into by the Commission pursuant to subsection 170c or k of the Act.

5. "Person indemnified" means the licensee and any other person who may be liable for public liability.

6. "Public liability" means any legal liability arising out of or resulting from a nuclear incident, except (1) claims under State or Federal Workmen's Compensation Acts of employees of persons indemnified who are employed (a) at the location or, if the nuclear incident occurs in the course of transportation of the radioactive material, on the transporting vehicle, and (b) in connection with the licensee's possession, use, or transfer of the radioactive material; (2) claims arising out of an act of war; and (3) claims for loss of, or damage to, or loss of use of (a) property which is located at the location and used in connection with the licensee's possession, use, or transfer of the radioactive material, and (b) if the nuclear incident occurs in the course of transportation of the radioactive material, the transporting vehicle, containers used in such transportation, and the radioactive material.

7. "The location" means the location described in Item 3 of the Attachment hereto.

8. "The radioactive material" means source, special nuclear, and byproduct material which (1) is used or to be used in, or is irradiated or to be irradiated by, the nuclear reactor or reactors subject to the license or licenses designated in the Attachment hereto, or (2) is produced as the result of operation of said reactor(s).

9. "United States" when used in a geographical sense includes all Territories and possessions of the United States, the Canal Zone and Puerto Rico.

ARTICLE II

1. Any obligations of the licensee under subsection 53e(8) of the Act to indemnify the United States and the Commission from public liability shall not in the aggregate exceed $250,000 with respect to any nuclear incident.

2. With respect to any extraordinary nuclear occurrence to which this agreement applies, the Commission, and the licensee on behalf of itself and other persons indemnified, insofar as their interests appear, each agree to waive

(a) any issue or defense as to the conduct of the claimant or fault of persons indemnified, including, but not limited to

(1) negligence;

(2) contributory negligence;

(3) assumption of the risk;

(4) unforeseeable intervening causes, whether involving the conduct of a third person or an act of God.

As used herein, "conduct of the claimant" includes conduct of persons through whom the claimant derives his cause of action;

(b) any issue or defense as to charitable or governmental immunity;

(c) any issue or defense based on any statute of limitations if suit is instituted within three years from the date on which the claimant first knew, or reasonably could have known, of his injury or damage and the cause thereof, but in no event more than ten years after the date of the nuclear incident.

The waiver of any such issue or defense shall be effective regardless of whether such issue or defense may otherwise be deemed jurisdictional or relating to an element in the cause of action. The waivers shall be judicially enforceable in accordance with their terms by the claimant against the person indemnified.

3. The waivers set forth in paragraph 2 of this Article:

(a) shall not preclude a defense based upon a failure to take reasonable steps to mitigate damages;

(b) shall not apply to injury or damage to a claimant or to a claimant's property which is intentionally sustained by the claimant or which results from a nuclear incident intentionally and wrongfully caused by the claimant;

(c) shall not apply to injury to a claimant who is employed at the site of and in connection with the activity where the extraordinary nuclear occurrence takes place if benefits therefor are either payable or required to be provided under any workmen's compensation or occupational disease law;

(d) shall not apply to any claim for punitive or exemplary damages, provided, with respect to any claim for wrongful death under any State law which provides for damages only punitive in nature, this exclusion does not apply to the extent that the claimant has sustained actual damages, measured by the pecuniary injuries resulting from such death but not to exceed the maximum amount otherwise recoverable under such law;

(e) shall be effective only with respect to those obligations set forth in this agreement;

(f) shall not apply to, or prejudice the prosecution or defense of, any claim or portion of claim which is not within the protection afforded under (1) the limit of liability provisions under subsection 170e of the Atomic Energy Act of 1954, as amended, and (b) the terms of this agreement.

ARTICLE III

1. The Commission undertakes and agrees to indemnify and hold harmless the licensee and other persons indemnified, as their interest may appear, from public liability.

2. With respect to damage caused by a nuclear incident to property of any person legally liable for the nuclear incident, the Commission agrees to pay to such person those sums which such person would have been obligated to pay if such property had belonged to another; provided, that the obligation of the Commission under this paragraph 2 does not apply with respect to:

(a) Property which is located at the location and used in connection with the licensee's possession, use, or transfer of the radioactive material;

E

(b) Property damage due to the neglect of the person indemnified to use all reasonable means to save and preserve the property after knowledge of a nuclear incident;

(c) If the nuclear incident occurs in the course of transportation of the radioactive material, the transporting vehicle and containers used in such transportation;

(d) The radioactive material.

3. The Commission agrees to indemnify and hold harmless the licensee and other persons indemnified, as their interest may appear, from the reasonable costs of investigating, settling and defending claims for public liability.

4.(a) The obligations of the Commission under this agreement shall apply only with respect to such public liability, such damage to property of persons legally liable for the nuclear incident (other than such property described in the proviso to paragraph 2 of this Article) and such reasonable costs described in paragraph 3 of this Article as in the aggregate exceed $250,000.

(b) With respect to a common occurrence, the obligations of the Commission under this agreement shall apply only with respect to such public liability, such damage to property of persons legally liable for the nuclear incident (other than such property described in the proviso to paragraph 2 of this Article) and to such reasonable costs described in paragraph 3 of this Article as in the aggregate exceed whichever of the following is lower: (1) the sum of the amounts of financial protection established under all applicable agreements; or (2) $74,000,000. As used in this Article, "applicable agreements" means each agreement entered into by the Commission pursuant to subsection 170c of the Act in which agreement the nuclear incident is defined as a "common occurrence."

5. The obligations of the Commission under this agreement shall apply only with respect to nuclear incidents occurring during the term of this agreement.

6. The obligations of the Commission under this and all other agreements and contracts to which the Commission is a party shall not, with respect to any nuclear incident, in the aggregate exceed whichever of the following is the lower: (a) $500,000,000 or (b) with respect to a common occurrence, $560,000,000 less the sum of the amounts of financial protection established under all applicable agreements.

7. If the licensee is immune from public liability because it is a State agency, the Commission shall make payments under this agreement in the same manner and to the same extent as the Commission would be required to do if the licensee were not such a State agency.

8. The obligations of the Commission under this agreement, except to the licensee for damage to property of the licensee, shall not be affected by any failure on the part of the licensee to fulfill its obligations under this agreement. Bankruptcy or insolvency of the licensee or any other person indemnified or of the estate of the licensee or any other person indemnified shall not relieve the Commission of any of its obligations hereunder.

ARTICLE IV

1. When the Commission determines that the United States will probably be required to make indemnity payments under the provisions of this agreement, the Commission shall have the right to collaborate with the licensee and other persons indemnified in the settlement and defense of any claim and shall have the right (a) to require the prior approval of the Commission for the settlement or payment of any claim or action asserted against the licensee or other person indemnified for public liability or damage to property of persons legally liable for the nuclear incident which claim or action the licensee or the Commission may be required to indemnify under this agreement; and (b) to appear through the Attorney General of the United States on behalf of the licensee or other person indemnified, take charge of such action and settle or defend any such action. If the settlement or defense of any such action or claim is undertaken by the Commission, the licensee shall furnish all reasonable assistance in effecting a settlement or asserting a defense.

E

2. Neither this agreement nor any interest therein nor claim thereunder may be assigned or transferred without the approval of the Commission.

ARTICLE V

The parties agree that they will enter into appropriate amendments of this agreement to the extent that such amendments are required pursuant to the Atomic Energy Act of 1954, as amended, or licenses, regulations or orders of the Commission.

ARTICLE VI

The licensee agrees to pay to the Commission such fees as are established by the Commission pursuant to regulations or orders of the Commission.

ARTICLE VII

The term of this agreement shall commence as of the date and time specified in Item 4 of the Attachment and shall terminate at the time of expiration of that license specified in Item 2 of the Attachment, which is the last to expire; provided that, except as may otherwise be provided in applicable regulations or orders of the Commission, the term of this agreement shall not terminate until all the radioactive material has been removed from the location and transportation of the radioactive material from the location has ended as defined in subparagraph 4(b), Article I. Termination of the term of this agreement shall not affect any obligation of the licensee or any obligation of the Commission under this agreement with respect to any nuclear incident occurring during the term of this agreement.

UNITED STATES ATOMIC ENERGY COMMISSION

Indemnity Agreement No. E-39

ATTACHMENT

Item 1 - Licensee Massachusetts Institute of Technology

Address Cambridge, Massachusetts 02139

Item 2 - License number or numbers

R-37

Item 3 - Location

The Reactor Building with stack and cooling towers including the area circumscribed by a chain link fence on the north and south sides of said building; a concrete wall and chain link fence on the east side of said building; and a line coinciding with the east wall of the Nuclear Engineering Building (Room NW12). Also, that portion of the Nuclear Engineering Building north of the partition extending from the southeast corner of the Transformer Vault (Room 123) to the southwest corner of the Spectrometer Set-up Room (Room 119); and the fuel storage vault rooms identified as NW12-127, NW12-213 and NW12-313 and the connecting corridors and the elevator when nuclear fuels are being moved to and from the vaults and the areas first mentioned. The location is further depicted on the two prints, "Building NW12 and Reactor," dated May 1, 1964, and transmitted with the Institute's letter of May 7, 1964. Said prints are made part of this indemnity agreement by reference.

The above location is a portion of the facilities commonly known as 120 through 138 Albany Street, Cambridge, Massachusetts.

Item 4 - The indemnity agreement designated above, of which this Attachment is a part, is effective as of 12:01 a.m., on the 9th day of June 1958, and supersedes the interim indemnity agreement between the licensee and the Atomic Energy Commission dated May 25, 1959.

FOR THE UNITED STATES ATOMIC ENERGY COMMISSION

Eber R. Price, Director
Division of State and Licensee Relations

Accepted June 17, 1969

By COMPTROLLER
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

UNITED STATES
ATOMIC ENERGY COMMISSION
WASHINGTON, D.C. 20545

AMENDMENT TO INDEMNITY AGREEMENT NO. E- 39

AMENDMENT NO. 3

Effective February 1, 1969, Indemnity Agreement No. E- 39, between Massachusetts Institute of Technology and the Atomic Energy Commission, dated May 13, 1964, as amended, is hereby further amended as follows:

Article III, Paragraph 4(b)(2) is amended by deleting the amount "$74,000,000" and substituting therefor the amount "$82,000,000."

FOR THE UNITED STATES ATOMIC ENERGY COMMISSION

Eber R. Price, Director
Division of State and Licensee Relations

Accepted June 17, 1969

By COMPTROLLER
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

UNITED STATES
ATOMIC ENERGY COMMISSION
WASHINGTON, D.C. 20545

Docket No. 50-20

AMENDMENT TO INDEMNITY AGREEMENT NO. E-39

AMENDMENT NO. 4

Effective December 14, 1971, Indemnity Agreement No. E-39 between Massachusetts Institute of Technology and the Atomic Energy Commission, dated May 13, 1964, as amended, is hereby further amended as follows:

Article II is amended by adding the following proviso at the end of subparagraph 3(c):

"Provided, however, that with respect to an extraordinary nuclear occurrence occurring at the facility, a claimant who is employed at the facility in connection with the construction of a nuclear reactor with respect to which no operating license has been issued by the Atomic Energy Commission shall not be considered as employed in connection with the activity where the extraordinary nuclear occurrence takes place if:

(1) the claimant is employed exclusively in connection with the construction of a nuclear reactor, including all related equipment and installations at the facility, and

(2) no operating license has been issued by the AEC with respect to the nuclear reactor, and

(3) the claimant is not employed in connection with the possession, storage, use or transfer of nuclear material at the facility."

FOR THE UNITED STATES ATOMIC ENERGY COMMISSION

Lyall Johnson, Director
Division of State and Licensee Relations

Accepted January 11, 1971

By
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
Vice President-Business & Fiscal Relations

RECEIVED
JAN 12
MIT REACTOR
138 ALBANY ST., CAMBRIDGE

UNITED STATES
ATOMIC ENERGY COMMISSION
WASHINGTON, D.C. 20545

Docket No. 50-20

AMENDMENT TO INDEMNITY AGREEMENT NO. E-39

AMENDMENT NO. 5

Effective March 1, 1972, Indemnity Agreement No. E-39, between Massachusetts Institute of Technology and the Atomic Energy Commission, dated May 13, 1964, as amended, is hereby further amended as follows:

Article III, Paragraph 4(b)(2) is amended by deleting the amount "$82,000,000" and substituting therefor the amount "$95,000,000."

FOR THE UNITED STATES ATOMIC ENERGY COMMISSION

Jerome Saltzman, Chief
Indemnity and Export Control Branch
Division of State and Licensee Relations

Accepted April 14, 1972

By
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
COMPTROLLER

UNITED STATES
ATOMIC ENERGY COMMISSION
WASHINGTON, D.C. 20545

Docket No. 50-20

AMENDMENT TO INDEMNITY AGREEMENT NO. E-39

AMENDMENT NO. 6

Effective MAY 24 1972, Indemnity Agreement No. E-39, between Massachusetts Institute of Technology and the Atomic Energy Commission, dated May 13, 1964, as amended, is hereby further amended as follows:

Item 3 of the Attachment to the indemnity agreement is amended by adding the following at the end:

"The location also includes Rooms NW12-139 and NW12-133, to the extent that such rooms are used in connection with activities licensed under Facility License R-37."

FOR THE UNITED STATES ATOMIC ENERGY COMMISSION

Jerome Saltzman, Assistant Chief
Office of Antitrust and Indemnity

APPROVED

Accepted JUN 14 1972, 1972

By
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
Paul V. Cusick
Vice President for business
and Fiscal Relations

MIT Copy

UNITED STATES
ATOMIC ENERGY COMMISSION
WASHINGTON, D.C. 20545

RECEIVED
MAR 28 1974
MIT REACTOR
138 ALBANY ST., CAMBRIDGE

Docket No. 50-20

File

AMENDMENT TO INDEMNITY AGREEMENT NO. E-39

AMENDMENT NO. 7

Effective March 1, 1974, Indemnity Agreement No. E-39, between Massachusetts Institute of Technology and the Atomic Energy Commission, dated May 13, 1964, as amended, is hereby further amended as follows:

Article III, Paragraph 4(b)(2) is amended by deleting the amount "$95,000,000" and substituting therefor the amount "$110,000,000."

FOR THE UNITED STATES ATOMIC ENERGY COMMISSION

Jerome Saltzman, Deputy Chief
Office of Antitrust & Indemnity
Directorate of Licensing

Accepted MAR 25 [illegible], 1974

By Stuart H Cowen KV
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
Stuart H. Cowen Vice President for Financial Operations

UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D. C. 20555

RECEIVED APR 1 1975

Docket No. 50-20

AMENDMENT TO INDEMNITY AGREEMENT NO. E-39

AMENDMENT NO. 8

Effective March 21, 1975, Indemnity Agreement No. E-39, between Massachusetts Institute of Technology, and the Atomic Energy Commission, dated May 13, 1964, as amended, is hereby further amended as follows:

> The name "United States Atomic Energy Commission" is deleted wherever it appears and the name "United States Nuclear Regulatory Commission" is substituted therefor.
>
> Article III, Paragraph 4(b)(2) is amended by deleting the amount "$110,000,000" and substituting therefor the amount "$125,000,000."

FOR THE UNITED STATES NUCLEAR REGULATORY COMMISSION

Jerome Saltzman, Deputy Chief
Office of Antitrust & Indemnity
Nuclear Reactor Regulation

Accepted March 27, 1975
STUART H. COWEN
Vice President For Financial Operations
By ________________________
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

AMERICAN REVOLUTION BICENTENNIAL 1776-1976

3489

UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D. C. 20555

Docket No. 50-20

AMENDMENT TO INDEMNITY AGREEMENT NO. E-39

AMENDMENT NO. 9

Effective MAY 1 1977, Indemnity Agreement No. E-39, between Massachusetts Institute of Technology, and the Atomic Energy Commission, dated May 13, 1964, as amended, is hereby further amended as follows:

Article III, Paragraph 4(b)(2) is amended by deleting the amount "125,000,000" and substituting therefor the amount "140,000,000."

FOR THE UNITED STATES NUCLEAR REGULATORY COMMISSION

Jerome Saltzman, Chief
Antitrust & Indemnity Group
Nuclear Reactor Regulation

Accepted May 25, 1977

By Kimball Valentine
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
INSURANCE AND LEGAL ADMINISTRATION OFFICER

UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D. C. 20555

Docket No. 50-20

AMENDMENT TO INDEMNITY AGREEMENT NO. E-39

AMENDMENT NO. 10

Effective May 1, 1979, Indemnity Agreement No. E-39, between Massachusetts Institute of Technology and the Atomic Energy Commission, dated May 13, 1964, as amended, is hereby further amended as follows:

Article III, Paragraph 4(b)(2) is amended by deleting the amount "$140,000,000" and substituting therefor the amount "$160,000,000."

FOR THE UNITED STATES NUCLEAR REGULATORY COMMISSION

Jerome Saltzman, Chief
Antitrust and Indemnity Group
Office of Nuclear Reactor Regulation

Accepted June 4, 1979

By Kimball Valentine
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D. C. 20555

Docket No. 50-20

AMENDMENT TO INDEMNITY AGREEMENT NO. E-39

AMENDMENT NO. 11

Effective May 1, 1977, Indemnity Agreement No. E-39, between Massachusetts Institute of Technology, and the Atomic Energy Commission, dated May 13, 1964, as amended, is hereby further amended by modifying the prefatory language of paragraph 4, Article I, to read as follows:

> "In the course of transportation" means in the course of transportation within the United States, or in the course of transportation outside the United States and any other nation, including handling or temporary storage incidental thereto, of the radioactive material to the location or from the location provided that:

FOR THE UNITED STATES NUCLEAR REGULATORY COMMISSION

Jerome Saltzman, Chief
Antitrust & Indemnity Group
Office of Nuclear Reactor Regulation

Accepted October 31, 1979, 1979

By ______________________________
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D. C. 20555

Docket No. 50-20

Amendment to Indemnity Agreement No. E-39
Amendment No. 12

Effective July 1, 1989, Indemnity Agreement No. E-39 between Massachusetts Institute of Technology, and the Atomic Energy Commission, dated May 13, 1964, as amended, is hereby further amended as follows:

The amount "$160,000,000" is deleted wherever it appears and the amount "$200,000,000" is substituted therefor.

The amount "$124,000,000" is deleted wherever it appears and the amount "$155,000,000" is substituted therefor.

The amount "$36,000,000" is deleted wherever it appears and the amount "$45,000,000" is substituted therefor.

Paragraph 1, Article I is modified to read as follows:

1. "Nuclear reactor," "byproduct material," "person," "source material," "special nuclear material," and "precautionary evacuation" shall have the meanings given them in the Atomic Energy Act of 1954, as amended, and the regulations issued by the Commission.

The definition of "public liability" in paragraph 7, Article I is deleted, and the following is substituted therefor:

"Public liability" means any legal liability arising out of or resulting from a nuclear incident or precautionary evacuation (including all reasonable additional costs incurred by a State or a political subdivision of a State, in the course or responding to a nuclear incident or precautionary evacuation), except (1) claims under State or Federal Workmen's Compensation Acts of employees of persons indemnified who are employed (a) at the location or, if the nuclear incident occurs in the course of transportation of the radioactive material, on the transporting vehicle, and (b) in connection with the licensee's possession, use or transfer of the radioactive material; (2) claims arising out of an act of war; and (3) claims for loss of, or damage to, or loss of use of (a) property which is located at the location and used in connection with the licensee's possession, use, or transfer of the radioactive material, and (b) if the nuclear incident occurs in the course of transportation of the radioactive material, the transporting vehicle, containers used in such transportation, and the radioactive material.

Paragraph 4(c), Article II is revised to read as follows:

(c) Any issue or defense based on any statute of limitations if suit is instituted within three years from the date on which the claimant first knew, or reasonably could have known, of his injury or damage and the cause thereof.

Paragraph 1, Article IV is revised to read as follows:

1. When the Commission determines that the United States will probably be required to make indemnity payments under the provisions of this agreement, the Commission shall have the right to collaborate with the licensee and other persons indemnified in the settlement and defense of any claim (including such legal costs of the license as are approved by the Commission) and shall have the right (a) to require the prior approval of the Commission for the settlement or payment of any claim or action asserted against the licensee or other person indemnified for public liability or damage to property of persons legally liable for the nuclear incident which claim or action the licensee or the Commission may be required to indemnify under this agreement; and (b) to appear through the Attorney General of the United States on behalf of the licensee or other person indemnified, take charge of such action and settle or defend any such action. If the settlement or defense of any such action or claim is undertaken by the Commission, the licensee shall furnish all reasonable assistance in effecting a settlement or asserting a defense.

In paragraph 1, Article VIII, the amount "$5,000,000" is deleted and the amount "$63,000,000" is substituted therefor.

FOR THE U.S. NUCLEAR REGULATORY COMMISSION

Cecil O. Thomas

Cecil O. Thomas, Chief
Policy Development and Technical Support Branch
Program Management Policy Development
and Analysis Staff
Office Nuclear Reactor Regulation

Accepted May 21, 1990

By Thomas R. Hennessey
Massachusetts Institute of Technology

IN THE UNITED STATES COURT OF FEDERAL CLAIMS

WILLIAM H. SWEET, M.D., and **MASSACHUSETTS INSTITUTE OF TECHNOLOGY** **Plaintiffs** **v.** **THE UNITED STATES** **Defendant**	))))))))	**Nos. 00-274C, 00-292C** **(Judge Firestone)**

AFFIDAVIT OF MIT'S COUNSEL, OWEN GALLAGHER

I, Owen Gallagher, aver:

I am counsel for the Massachusetts Institute of Technology ("MIT") in the present case. I represented MIT in the underlying matter of *Heinrich, et al v. Sweet, et al.*, Civil Action No. 97-CIV-12134-WGY, which was tried in the United States District Court for the District of Massachusetts. The following attached documents were admitted as evidence in the *Heinrich v. Sweet* matter.

1. Final Hazards Summary Report to the Commission's Advisory Committee on Reactor Safeguards dated January 1956 (Trial Exhibit No. 2).

2. License No. R-37 and Findings and Conclusions of the Atomic Energy Commission (Trial Exhibit No. 110)

3. Memorandum from James F. Haggerty, Medical Research Branch of the Division of Biology and Medicine regarding Visit Report to Massachusetts General Hospital, June 19, 1959 (Trial Exhibit No. 36).

4. Document submitted by MIT with its license application to the Atomic Energy Commission (Trial Exhibit No. 8).

5. Selected portions of Thesis by John-Ho Richard Choi, "Development and Characterization of an Epithermal Beam for Boron Neutron Capture Therapy at the MITR-II Research Reactor" dated April 1991. (Selected portions of Trial Exhibit No. 29).

6. Asbury, Arthur K., et al., "Neuropathologic Study of Fourteen Cases of Malignant Brain Tumor Treated by Boron-10 Slow Neutron Capture Radiation", Journal of Neuropathology and Experimental Neurology, Vol. XXXI, No. 2, pp. 278-303 (April 1972) (Trial Exhibit No. 1).

Signed under the pains and penalties of perjury this 5th day of April, 2001.

Owen Gallagher (BBO #183420)
GALLAGHER & GALLAGHER, P.C.
120 2nd Avenue
Boston, MA 02129
617-598-3800

FINAL HAZARDS SUMMARY REPORT TO THE ADVISORY COMMITTEE ON REACTOR SAFEGUARDS ON A RESEARCH REACTOR FOR THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY

January 1956

Massachusetts Institute of Technology
Cambridge, Mass.

4 pneumatic sample changers
6 3-inch vertical sample tubes in the graphite
1 thermal column including two side ports in line, one vertical port and three front ports
1 medical therapy facility

Those facilities will be used to perform many types of experiments including the following:

1. Neutron diffraction experiments primarily to provide data for a solid-state physics research program.

2. Horizontal beam experiments on neutron scattering, cross sections, etc.

3. The development of neutron beam therapy as a method of treatment of cancer, and other medical research.

4. Exponential assemblies to assist in the instructional program in nuclear engineering.

5. Irradiation of samples for use in food technology, radiochemistry, mechanical engineering, biology, chemical engineering, and nuclear engineering.

6. Capture gamma experiments to aid in fundamental investigations of the properties of the nucleus.

VII. Hazards and Accidents

It has been postulated in this report that the maximum credible accident is the sudden addition of a fuel element in the center of the just-critical reactor. The increase in reactivity caused by this accident is 2.3%. If all of the scram and safety mechanisms fail to operate, the reactor power will rise on a period of 40 milliseconds. Boiling will occur within the fuel elements. This boiling will limit the reactor power and the reactor will either "bump" or boil steadily. In the normal course of events several control elements would have to be out of the reactor for this accident to occur. Under these circumstances, D_2O steam will boil out of the top holes until the lowering of the D_2O level cuts off the reactor. In the remote event that the lid were to be fully sealed, at the time of this incident, the D_2O pressure would build up until the blowout patch on the D_2O storage tank gave way or, at worst, the reactor tank ruptured.

Exhibit 110

UNITED STATES
ATOMIC ENERGY COMMISSION
WASHINGTON 25, D. C.

DOCKET NO. 50-20
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

L I C E N S E

License No. R-37

1. Subject to the conditions and requirements incorporated herein, the Commission hereby licenses Massachusetts Institute of Technology (hereinafter referred to as "MIT"):

   a. Pursuant to Section 104a. and c. of the Atomic Energy Act of 1954 as amended, and Title 10, CFR, Chapter 1, Part 50, "Licensing of Production and Utilization Facilities", to possess and operate as a utilization facility the nuclear research reactor facility (hereinafter "the facility") designated below;

   b. Pursuant to the Act and Title 10, CFR, Chapter 1, Part 70, "Special Nuclear Material", to receive, possess and use 12 kilograms of uranium enriched to approximately 93% in the uranium 235 isotope as fuel for operation of the facility.

   c. Pursuant to the Act and Title 10, CFR, Chapter 1, Part 30, "Licensing of Byproduct Material", to possess, but not to separate, such byproduct material as may be produced in the operation of the facility.

2. This license applies to the facility which is owned by MIT and located in Cambridge, Massachusetts, and described in MIT's application filed on February 20, 1956, and amendments to the application, filed on May 1[illegible], 1957, September 16, 1957, November 27, 1957, January 2, 1958, January 9, 1958, January 27, 1958, February 24, 1958, and March 2[illegible], 1958, (hereinafter "the application"). The reactor is a one megawatt (thermal) heavy water-cooled and -moderated, heterogeneous, enriched uranium reactor. Experimental facilities are provided for use in neutron diffraction work, horizontal beam experiments, neutron beam therapy experiments, exponential assembly experiments, and neutron irradiation studies.

3. This license shall be deemed to contain and be subject to the conditions specified in Section 50.54 of Part 50 and Section 70.32 of Part 70; is subject to all applicable provisions of the Act and rules, regulations and orders of the Commission now or hereafter in effect; and is subject to the additional conditions specified or incorporated below.

EXHIBIT

ZO

a. Operating Restrictions

(1) MIT shall operate the facility in accordance with the procedures and limitations described in the application.

(2) MIT shall not operate the facility at a power level in excess of 1000 kilowatts (thermal).

(3) No experiment shall be introduced into or permitted to remain in the reactor if more than one per cent excess reactivity would be introduced into the reactor by the withdrawal or loss of that experiment.

(4) The reactor shall not be operated at a power level in excess of that necessary to measure the temperature and void coefficients until MIT has measured these coefficients and found them to be of the sign, and substantially of the magnitude, calculated in its application.

b. Records

In addition to those otherwise required under this license and applicable regulations, MIT shall keep the following records:

(1) Facility operating records, including power levels.

(2) Records showing radioactivity released or discharged into the air or water beyond the effective control of MIT as measured at the point of such release or discharge.

(3) Records of emergency scrams, including reasons for emergency shutdowns.

c. Reports

(1) MIT shall immediately report to the Commission any indication or occurrence of a possible unsafe condition relating to the operation of the facility.

(2) MIT shall, upon completion of the start-up experiments described in its application, submit a report to the Commission describing such experiments and the results thereof.

4. Pursuant to Section 50.60 of the regulations in Title 10, Chapter 1, CFR, Part 50, the Commission has allocated to MIT, for use in the operation of the reactor, 11.63 kilograms of uranium 235 contained in uranium (enriched to approximately 93% in the isotope uranium 235). Estimated schedules of special nuclear material transfers to MIT and returns to the Commission are contained in Appendix "A" which is attached hereto. Shipments by the Commission to MIT in accordance with column 2 in Appendix "A" will be conditioned upon MIT's return to the Commission of material substantially in accordance with column 3 of Appendix "A".

5. This license is effective as of the date of issuance and shall expire at midnight May 7, 1996, unless sooner terminated.

FOR THE ATOMIC ENERGY COMMISSION

H. L. Price
Director
Division of Licensing and Regulation

Date of Issuance: JUN [illegible] 1966

APPENDIX "A"

TO

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

FACILITY LICENSE

Estimated Schedule of Transfers of Special Nuclear Material from the Commission to Massachusetts Institute of Technology and to the Commission from MIT:

(1) Date of Transfer (Fiscal Year)	(2) Transfers from AEC to MIT Kgs. U-235	(3) Returns by MIT to AEC Kgs. U-235 Recoverable Cold Scrap	(3) Returns by MIT to AEC Kgs. U-235 Spent Hot Fuel	(4) Net Yearly Distribution Including Cumulative Losses Kgs. U-235	(5) Cumulative Distribution Including Cumulative Losses Kgs. U-235
1957	5.00	-	-	5.00	5.00
1958	1.04	3.04	0.92	(2.92)	2.08
1959	3.33	1.66	1.37	0.30	2.38
1960	2.50	1.25	1.00	0.25	2.63

In years 1960 through 1996 columns (2) through (4) carry the same quantities. Column (5) increases by 0.25 Kg. each year.

1996	2.50	1.25	1.00	0.25	11.63
Inventory to be returned	-	-	2.23	(2.23)	9.40
	101.[illegible]	50.95	41.52	9.40	

MIT 1002626

IN THE MATTER OF)
MASSACHUSETTS INSTITUTE OF)
TECHNOLOGY)

Docket No. 50-20

FINDINGS AND CONCLUSIONS

A. Findings

1. On February 20, 1956, the Massachusetts Institute of Technology (hereinafter referred to as MIT) submitted an application for the necessary licenses to construct and operate a research reactor.

2. MIT is a nonprofit, private, educational institution organized under the laws of the State of Massachusetts. MIT is not owned, controlled, or dominated by an alien, foreign corporation, or foreign government.

3. The MIT reactor is a one megawatt (thermal) heavy water-cooled and -moderated, heterogeneous, enriched uranium reactor. The reactor is to be used for the conduct of research. Experimental facilities are provided for use in neutron diffraction work, horizontal beam experiments, neutron beam therapy experiments, exponential assembly experiments, and neutron irradiation studies.

   The reactor core and the heavy water moderator are contained in an aluminum pressure vessel. The experimental facilities located outside of the pressure vessel in the graphite reflector, consist of horizontal ports, rotary changing ports, instrument ports, pneumatic tube changers, thimble tubes, thermal columns, and a medical therapy radiation facility. The only experimental facilities located inside of the pressure vessel are six small sample tubes in the heavy water moderator.

   The fuel consists of 19 curved plate-type fuel elements, similar to those in the Materials Testing Reactor at Arco, Idaho.

   For control and regulation of the reactor, there are six top entry shim-safety rods which penetrate vertically through seals in the pressure vessel into the core region. The control rod drive mechanisms are located between two concrete plugs at the top of the reactor tank.

   The pressure vessel for this reactor is an aluminum cylinder 4 feet in diameter and $\frac{3}{4}$ inch thick. This vessel was designed to be in accordance with the ASME Code for Unfired Pressure Vessels to withstand a pressure of 40 psig. The top lid of the pressure vessel is designed to withstand 80 psig. The pressure vessel is surrounded by two feet of graphite. The graphite is enclosed in a boral-lined steel gas-tight container. Outside of this container is a water-cooled thermal shield consisting of a layer of steel and lead. Surrounding the thermal shield is a layer of high density concrete about six feet thick which serves as the biological shield.

   The coolant system consists of a primary heavy water loop heat exchanger, a secondary light water loop, and a cooling tower in the secondary loop. The coolant pipes enter at the bottom of the pressure vessel and circulate upward through the core.

MIT 1002627

4. On May 7, 1956, the AEC issued Construction Permit No. CPRR-5 to MIT for the construction of the reactor for which they are now seeking an operating license.

5. The construction permit CPRR-5 provides that "MIT is financially qualified to construct and operate the reactor in accordance with the regulations contained in Title 10, Chapter 1, Code of Federal Regulations; to assume financial responsibility for the payment of Commission charges for special nuclear material and to undertake and carry out the proposed use of such material for a reasonable period of time." There has been no information developed with respect to the financial qualifications of MIT which significantly changes the facts upon which this conclusion was based.

6. The Massachusetts Institute of Technology has had many years experience in conducting a program of instruction and experimentation in the field of nuclear engineering and related subjects. The MIT staff is well trained in the theoretical aspects of reactor operation and several members of the staff have had operating experience with reactors.

7. The construction permit specified certain additional information required of the applicant prior to the issuance of the operating license. Such information included:

"(a) A standard operating procedure, including start-up routine and non-routine operation, and shut-down;

"(b) A description of critical experiments to be performed, including procedures to be followed; and

"(c) A plan of action for disaster control in event of accident or incident resulting in a radioactive hazard to the public."

Information on these matters has been supplied and is discussed in Findings Number 8, 9, and 10, respectively.

8. During the initial start-up the reactor coolant system is to be filled with light water and flow tests are to be conducted using primarily dummy fuel elements. After these tests are completed, the fuel elements are to be removed and the reactor is to be drained, dried and then filled with heavy water. Checks are then to be made to insure that all operating conditions, instrumentation and controls, experimental facilities and safety systems are in proper order.

The reactor is to be operated five days per week. At the beginning of each operating period all safety systems are to be checked and, if necessary, a new fuel element is to be loaded. Each time a new loading has been made, an experiment is to be performed to determine the critical position of shim and control rods.

The applicant has established operating rules for this facility including administrative regulations for routine and emergency procedures, procedures for reviewing reactor experiments, and procedures for determining the qualification and responsibilities of operators.

The proposed operating procedures appear to be adequate to provide reasonable assurance that the reactor can be operated safely.

9. MIT is to conduct a number of initial critical experiments including cali- bration of shim rods, regulating rod, heavy water level, and neutron absorbers; oscillation frequency experiments; reactivity experiments involving non-uniform loadings, neutron flux and spectral distribution measurements; radiation surveys; fission product poisoning measurements; instrumentation adjustments and cali- brations; temperature distribution measurements; temperature and void coef- ficient measurements; and general performance, inspection, checks and tests with simulation of possible failures. The experiments described and the means for conducting such experiments appear adequate to provide the neces- sary initial operating data.

10. MIT has established a detailed disaster control plan. This plan provides for the evacuation of people under the immediate control of MIT and for immediate liaison, where necessary, with appropriate State and local officials. This plan appears adequate [illegible] for emergency situ- ations.

11. The reactor is located in a [illegible] containment building. The building has been designed in accordance with the American Petroleum Institute Recom- mended Rules for Large Welded Low-Pressure Storage Tanks to withstand an internal pressure of 1 psi. A concrete shadow shield [illegible] feet thick and [illegible] feet high surrounds the interior of the containment building.

The containment building is penetrated by a personnel air-lock, a truck air-lock, an inlet air duct, an aluminum neutron [illegible]dow, a [illegible] plug storage tank, two hydraulic lifts, an exhaust air [illegible], an emergency escape air-lock and several pipes and conduits. MIT is providing in both the inlet and outlet lines of the ventilation system for [illegible] automatically controlled valve, and a manually operat[illegible] valve in series.

The control mechanisms [illegible]vided at the [illegible] of penetrations in the containment building and the [illegible] and frequency of proposed leakage tests appear adequate to provide reasonable assurance that the leakage rate specified will be maintained. The leakage of the building will be measured after all penetrations have been installed and there will be [illegible] tests for leak tightness.

The construction permit approved the substitution of a single steel door in place of the truck air-lock in the containment building subject to two conditions. These conditions are not relevant since MIT has constructed the reactor with the truck air-lock. The air lock is adequate.

12. The MIT reactor is generally similar to the [illegible] research reactor at Argonne National Laboratory and should exhibit similar characteristics [illegible] negative temperature and void coefficients and a [illegible] neutron lifetime which are characteristic of a [illegible] of this general design concept [illegible] a high degree of inherent stability.

The temperature and void coefficients are expected to be sufficiently negative to assure safe operation. However, the information on which this finding is based consists of theoretical calculations. The sign and magnitude of these coefficients cannot be definitively established until measurements are made during actual operation of the reactor.

13. The maximum credible accident for this facility consists of the instantaneous insertion of not more than 2.3% excess reactivity. MIT has stated that such an insertion of excess reactivity could be caused by dropping a fuel element into the central fuel element position in the core of the reactor. The initiating mechanisms for this accident would require a combination of circumstances the concurrent occurrence of which are highly improbable.

The instantaneous insertion of 2.3% excess reactivity would place the reactor on a period of approximately 40 milliseconds. Based on the postulated thermal characteristics and temperature coefficient values for the MIT reactor, the temperature reached in the fuel is calculated to be well below the melting point of the fuel. The resulting excursion would be terminated by inherent shutdown characteristics of the core itself before any significant damage would result to the reactor.

Based upon information presently available, the acceptance of this accident as the maximum credible accident is dependent upon a limitation of the amount of excess reactivity which can be inserted by the loss of a single experiment. MIT has calculated that the amount of excess reactivity which could be added to the reactor as a result of flooding all of the experimental facilities with light water would be approximately 1%. Such flooding could credibly occur concurrently with the loss of a single experiment.

14. The greatest possible release of fission products under the conditions of containment specified for this facility from accidental spillage in the handling of the largest experiment to be conducted in this facility would be considerably less than 1.5 r of gamma radiation and an integrated dose of 92 rep to the thyroid from iodine 131 to a person continuously exposed at the site boundary for one hour. While a release of sufficient magnitude to result in such exposures is highly unlikely, these doses would not result in any clinically observable damage to those exposed.

15. MIT has submitted data describing the control and safety instrumentation and the administrative procedures relating to the use of the facility for neutron beam therapy experiments and medical therapy. The instrumentation and procedures appear to provide adequate protection for the health and safety of the public and personnel participating in the use of the facility for these purposes.

16. On January 27, 1958, MIT filed with the Commission as proof of financial protection pursuant to 10 C.F.R., Part 140, copies of binder No. 14, issued by Mutual Atomic Energy Liability Underwriters, covering this facility in the amount of $2,000,000.

17. The application has been referred to the Advisory Committee on Reactor Safeguards for a report with respect to the hazards of the facility. The report of the Committee has been made available to the public.

15. The AEC staff and the Commission's Advisory Committee on Reactor Safeguards believe that the MIT reactor can be operated with an acceptable degree of risk to the health and safety of the public. The advisory Committee recommended that provision be made for an auxiliary system of closing the inlet and outlet lines of the ventilation system. Since the ACRS considered this matter, MIT has stated that it will provide an adequate manually operated valve which is auxiliary to the automatically controlled valve now installed, prior to commencement of the research program.

B. Conclusions

1. The processes to be performed, the operating procedures, the facility and equipment, the use of the facility and other technical specifications provide reasonable assurance that the applicant will comply with the regulations in Chapter 1 of Title 10 of the Code of Federal Regulations, including the regulations in Part 20, and that the health and safety of the public will not be endangered by the operation of this facility, subject to the following conditions:

   (a) No experiment shall be introduced into or permitted to remain in the reactor if more than one per cent excess reactivity would be introduced into the reactor by the withdrawal or loss of that experiment.

   (b) The reactor shall not be operated at a power level in excess of that necessary to measure the temperature and void coefficients until MIT has measured these coefficients and found them to be of the sign, and substantially of the magnitude, calculated in its application.

2. MIT is technically qualified to operate the proposed reactor.

3. MIT is financially qualified to operate the reactor in accordance with the regulations contained in Title 10, Chapter 1, of the Code of Federal Regulations, and to assume financial responsibility for the payment of Commission charges for special nuclear material and to undertake and carry out the proposed use of such material for a reasonable period of time.

4. MIT has submitted proof of financial protection which satisfies the requirements of Commission regulations which are currently in effect.

5. The issuance of a license will not be inimical to the common defense and security or to the health and safety of the public.

FOR THE ATOMIC ENERGY COMMISSION

H. L. Price
Director
Division of Licensing and Regulation

720126

Files

~~July 10, 1959~~

James F. Haggerty, Medical Research Branch
Division of Biology and Medicine

VISIT REPORT TO MASSACHUSETTS GENERAL HOSPITAL
DR. WILLIAM SWEET, JUNE 19, 1959

SYMBOL: BMM:JFH

On Friday, June 19, 1959, a Task Force visit made up of Drs. Van Cleave, Henshaw, Spikes and Haggerty, and Mr. Stanwood, visited the research programs under the over-all cognizance of Dr. William Sweet at the Massachusetts General Hospital. This visit really covered three contracts, the first of which is under the immediate direction of Dr. Fernandez-Moran. Dr. Moran's primary interests are presently focused on electron microscopy of nervous tissue. To say we were quite amazed at the accomplishments, imagination, skill and competence of Dr. Fernandez-Moran is an understatement. We came away feeling that this man is positively a genius. He alone has done in a period of relatively few months what others have attempted to do over a period of years. He not only has an agile mind as far as research investigation is concerned, but he likewise has the capability of not only developing but actually building intricate electronic and tissue handling equipment. Each one of us was amazed at the accomplishments this man has made.

Dr. Sweet, in course of our visit, discussed his research concerned with brain tumor localization in patients and mentioned the increasing success he has had in detecting and delineating intracranial lesions. Though the majority of his scans have been accomplished with the use of AS 74, he has used a good deal of CU 64. Both he and Dr. Brownell definitely favor the use of arsenic. The coincidence counting apparatus has been functioning very satisfactorily and Dr. Brownell continues to improve its resolution.

Dr. Sweet's work with boron in relation to brain tumor therapy has had some rough going. He has been pushing hard on the chemical side of boron containing organic compounds and Dr. Albert Soloway brought us up to date on the compounds he has been working with. I might point out that this is one instance where a one-day conference has borne fruit. Dr. Soloway has established some very productive contacts as a result of the meeting held in Chicago, September 1958, sponsored by the Division of Biology and Medicine through AIBS.

Dr. Sweet took us through the MIT reactor which has a medical port at the base of the reactor. We detected considerable disappointment with respect to ultimate functioning of the port for Dr. Sweet indicated it would be several months before he could treat his first patient in the reactor. Though the first patients will be brain tumor patients he mentioned he is thinking toward the possibility of irradiating the pituitary for total ablation in certain advanced breast cancer patients. By inserting a needle containing a boron solution through the patient's nose, it is a fairly simple matter to hit the pituitary. Dr. Sweet gave us a very vivid demonstration on a cadaver.

We completed our visit here with the feeling that this is an excellent research program and deserving of Commission support at the present level or possibly at an increased level.

cc: Dr. Shilling
Betty Hower
New York Operations Office

OFFICE ▶	BMM				
SURNAME ▶	JFBeKarty:cw	ORGANIZATION & MANAGEMENT	15-1		
DATE ▶	6/6/59				

Form AEC-318 (Rev. 9-53) U. S. GOVERNMENT PRINTING OFFICE 16—62761-3

Fil Span Copies

The MIT Reactor Medical Facility

General

A facility is included in the MIT Reactor for irradiation of biological specimens, or patients. The main feature of this facility is a surgical operating room beneath the reactor. An opening in the concrete shielding allows a neutron and gamma ray beam to stream downward into the operating room. The design goal for this beam is 10^{10} thermal neutrons per cm^2 per second with less than 10^7 fast neutrons per cm^2 per second and less than 100 R/hour incident gamma flux. The room itself is shielded by four feet of concrete on all sides, except for a transparent shielding window and the door opening. The door opening is shielded by a lead door.

The neutron beam will be utilized in several different ways. Its most important use will be as a thermal neutron source for studies of cancer treatment in human patients. It will also be utilized for other biological and general experiments. In all cases the beam size will be reduced to the minimum compatible with the area to be irradiated. Normally external shielding at the exit of the lower shutter will further restrict the radiation so as to minimize hazards to the doctors and experimenters. To calibrate the beam a neutron spectrometer is being built. This will be shielded in such a way that personnel can work in the therapy room without danger from radiation.

The radiation beam is shut off when desired by a combination of three shutters. These include a water tank which may be filled or emptied, a boral shutter, and a lead shutter. In this manner the fast and thermal neutron doses, and the gamma radiation dose, can be reduced to low levels even with the reactor operating at full power. The shutter tank is emptied by pumping the water to a storage tank at the top of the reactor shield. The shutter tank is filled by deenergizing a solenoid valve, which then allows the water to drain by gravity back into the shutter tank. An interlock prevents the pump from running while the solenoid valve is open. The lead and boral shutters are normally operated by pneumatic

Exhibit 8

cylinders. Low air pressure causes the shutters to be closed automatically. An accumulator tank provides a reserve air supply. The shutters can also be closed manually from a position adjacent to the medical control center. Because of the manual closing method, the fail safe closing of the water shutter and the reserve air supply, the system is deemed adequate and, therefore, is not a part of the emergency power system.

Shutter Controls

Controls for the medical therapy shutters are located both inside the therapy room itself and outside at the medical therapy control panel adjacent to the shielding window.

The controls and indicators on the medical therapy control on outside consist of the following items:

1. Boral shutter
   a. "open" light
   b. "open" button
   c. "close" light
   d. "close" button
2. Lead shutter
   a. "open" light
   b. "open" button
   c. "close" light
   d. "close" button
3. Water shutter
   a. "open" light
   b. "open" button
   c. "hold" button (to partially fill tank)
   d. "close" button
   e. level indicating meter

(All of the above controls are activated by means of a key switch. When the key is removed these controls cannot be used.) In addition to the above items, there is a scram button which shuts the reactor off as well as closing all shutters. On this panel there is also a control for opening the door to the room.

The controls inside of the therapy room consist of duplicates of the controls and indicators listed above for the boral shutter and the lead shutter. The water shutter controls inside consist of a shutter "open" light and button, and a shutter "closed" light and button. The controls inside are activated by the same key switch mentioned above.

Radiation Monitoring

The basic radiation monitoring equipment consists of an ionization chamber mounted at one corner of the therapy room. This monitor switches automatically to the emergency power system. The radiation level is indicated and recorded continuously in the reactor control room.

In event of too high a radiation level in the therapy room the following indications are given:

1. a warning lamp at the monitor in the therapy room (This lamp is visible at the medical control panel.)
2. an illuminated radiation sign outside the room door
3. a flashing light on the annunciator panel and an alarm lamp on the radiation monitor panel in the reactor control room
4. an audible signal in the therapy room which may be muted if patients find it objectionable
5. an audible signal at the therapy control panel and in the control room

Therapy Room Door

When irradiating with an incompletely shielded beam the lead door at the entrance to the operating room will be closed. This door is motor driven and is normally controlled from pushbutton stations just inside and outside of the door. In an emergency the drive mechanism can be disconnected from either side of the door, and the door operated by hand. The only other way the door can be opened is by a button at the medical control panel. Lamps on the control room annunciator panel and at the medical control area will signal when the lead door is not closed. This door can be locked when the facility is not in use.

Since many of the experiments planned, including the initial calibration with the neutron spectrometer, will be fully shielded by portable shielding or integral shielding which will allow personnel to work in the area and take readings and make adjustments without radiation hazards, it is desirable that the room door not be interlocked with the shutters. An interlock door would require that the experiment be shut off for a period each time the door was opened. It would also require that the door be closed with personnel inside. Both of these aspects of the situation seem undesirable.

Adequate warning is afforded by the radiation warning lamp outside the door. The medical therapy control center receives indications of high radiation levels as well as of the door opening. The same signals are received and indicated prominently in the reactor control room. Thus, the entrance of anyone into this area would be observed normally by two separate control centers. Communications exist between both of these centers and the therapy room. With these precautions and problems in mind, no interlocks have been provided between the shutters and the door of the therapy room.

MIT Reactor Biomedical Advisory Committee

The ultimate responsibility for the performance and conduct of biomedical experiments at the MIT Reactor rests with MIT. However, since MIT is not a medical school, a committee has been formed to act in an advisory capacity for the review and approval of biomedical experiments to be conducted at the reactor.

This committee, the MIT Reactor Biomedical Advisory Committee, is composed of representatives from the three medical schools in the area, Boston University School of Medicine, Harvard Medical School, Tufts Medical School, and representatives from MIT. The functions of the committee are:

1. To review the biomedical experiments using reactor products and irradiation facilities at the reactor from the point of view of provision of maximum safety to investigators, patients, or any human beings on whom tracer experiments, diagnosis, or therapy is to be performed.

2. To consider the justification of the use of the reactor for the proposed biomedical experiments.
3. To acquaint the research and clinical groups in the surrounding area of the potentialities of the reactor and to encourage the use of reactor products and irradiation facilities by these groups at the reactor.

Proposals for biomedical experiments to be conducted at the reactor are to be submitted to the committee for review and approval. After review and formal approval of the proposal by the committee, the proposal will be submitted to the MIT Medical Department (Dr. James M. Faulkner, Director) for approval. The proposal will then be referred to the director and operating staff of the reactor project for further review and final approval.

Use of reactor products and irradiation facilities at the reactor for biomedical experiments involving human beings will not be authorized by the reactor project without the prior approval of the advisory committee and of the MIT Medical Department.

The advisory committee was formed early in 1957. The non-MIT members were appointed to the committee by the deans of the respective medical schools at the request of Dr. James M. Faulkner, Director, MIT Medical Department. The present membership of the committee is as follows: ✓

Dr. Arthur K. Solomon, Chairman
Associate Professor of Biophysics, Harvard Medical School; Consultant in Biophysics, Peter Bent Brigham Hospital; Consultant, Los Alamos Scientific Laboratory

Dr. Constantine Maletskos, Secretary
Radiation Biophysicist, Massachusetts Institute of Technology Medical Department; Radiation Protection Officer, Massachusetts Institute of Technology Reactor; Research Physicist, Radioactivity Center, Department of Physics, Massachusetts Institute of Technology

Dr. Hanson Benedict
Professor of Nuclear Engineering, Massachusetts Institute of Technology; Head, Nuclear Engineering Division, Department of Chemical Engineering, Massachusetts Institute of Technology; Member, Advisory Committee on Reactor Safeguards, Atomic MIT 1000093

Dr. Belton Burrows

Chief, Radioisotope Service, Boston Veteran's Administration Hospital; Assistant Professor of Medicine, Boston University School of Medicine; Associate Member, Evans Memorial Laboratory; Visiting Physician; Massachusetts Memorial Hospital ✓

Dr. Charles F. Emerson

Associate Professor of Medicine, Boston University School of Medicine; Director of Hematology, Evans Memorial Laboratory; Director Transfusion Services, Massachusetts Memorial Hospital; Associate Director, Radioisotope Laboratory, Massachusetts Memorial Hospital; Hematology Consultant, United States Public Health Hospital, Brighton, Massachusetts

Dr. Harriet Hardy

Assistant Medical Director, Massachusetts Institute of Technology; Head, Occupational Medical Service, Massachusetts Institute of Technology; Former Health Division Group Leader, Los Alamos Scientific Laboratory; Consultant, Division of Biology and Medicine, Atomic Energy Commission; Consultant, Los Alamos Scientific Laboratory; Consultant, Atomic Research Center, Ames, Iowa ✓

Dr. William Moloney

Clinical Professor of Medicine, Tufts; Director, Tufts Hematology Laboratory; Director, Clinical Laboratories, Boston City Hospital ✓

Dr. William Sweet

Associate Professor of Surgery, Harvard Medical School; Visiting Neurosurgeon, Massachusetts General Hospital; Former Regional Consultant, Midland Region and Neurosurgeon-in-chief, Queen Elizabeth Hospital, Birmingham, England ✓

Dr. Shields Warren

Professor of Pathology, Harvard Medical School; Director of Laboratory, New England Deaconess Hospital; Member, Advisory Committee on Biology and Medicine, Atomic Energy Commission; Formerly Head of Division of Biology and Medicine, Atomic Energy Commission, United States Representative to United Nations Science Committee on Effects of Atomic Radiation

Ex-officio member

Dr. James Faulkner

Professor and Medical Director, Massachusetts Institute of Technology Medical Department; Former Dean, Boston University School of Medicine; Professor of Clinical Medicine, Boston University School of Medicine; Diplomat, American Board of Internal Medicine; Fellow, American College of Physicians; Vice Chairman, Council on Medical Education and Hospitals, American Medical Association

DEVELOPMENT AND CHARACTERIZATION OF AN EPITHERMAL BEAM FOR BORON NEUTRON CAPTURE THERAPY AT THE MITR-II RESEARCH REACTOR

by

JONG-HO RICHARD CHOI

B.S., University of California, Berkeley
(1986)

M.S., University of California, Berkeley
(1987)

VOL I

SUBMITTED TO THE DEPARTMENT OF
NUCLEAR ENGINEERING IN PARTIAL FULFILLMENT OF
THE REQUIREMENT FOR THE DEGREE OF

DOCTOR OF SCIENCE

at the

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

April 1991

Signature of Author ______________________
Department of Nuclear Engineering
April 5, 1991

Certified by ______________________
Prof. Otto K. Harling
Thesis Supervisor

____
Dr. John A. Bernard
Thesis Reader

Accepted by ______________________
Prof. Allan F. Henry
Chairman, Departmental Graduate Committee

Exhibit 29
22981

EXHIBIT
JD

DEVELOPMENT AND CHARACTERIZATION OF AN EPITHERMAL BEAM FOR BORON NEUTRON CAPTURE THERAPY AT THE MITR-II RESEARCH REACTOR

by

JONG-HO RICHARD CHOI

Submitted to the Department of Nuclear Engineering on April 5, 1991 in partial fulfillment of the requirements for the Degree of Doctor of Science in Radiological Sciences

ABSTRACT

After looking at over 100 Monte Carlo based designs, and with the help of extensive hand calculations, over 40 different epithermal neutron beam filters were designed, fabricated, installed, and characterized through both paired ion chamber and activation foil measurements. This thesis describes in detail the performance of the currently available epithermal neutron beam at MITR-II. This beam, known as the M-055 beam, is one of the few clinically useful epithermal neutron beams available for BNCT in the world. The MITR-II epithermal neutron beam has a peak thermal neutron flux of greater than 4×10^8 n/cm^2 s at 2 cm depth in tissue. Assuming a B-10 concentration of 30 μg/g in tumor and an effective 10 to 1 ratio of B-10 in tumor to healthy tissue, the most important figures of merit for the beam are as follows. The advantage depth (useful therapeutic penetration) is in excess of 7 cm. The therapeutic dose rate at the advantage depth is 9.1 RBE cGy/min. The ratio of dose to tumor vs. dose to healthy tissue is greater than 3 when measured along the centerline of the ellipsoidal water phantom. When used in bilateral irradiation of the tumor, this beam can treat the entire brain with therapeutic advantage ratio of greater than 2.5.

In addition, plans for improving the current epithermal beam through straightforward modifications are presented. This improved beam is expected to have peak thermal neutron flux in excess of 10^9 n/cm^2 s with proportionally greater therapeutic dose rate and therapeutic ratio than the current M-055 epithermal neutron beam.

THESIS SUPERVISOR: PROF. OTTO K. HARLING
TITLE: PROFESSOR OF NUCLEAR ENGINEERING

THESIS READER: DR. JOHN A. BERNARD
TITLE: DIRECTOR OF REACTOR OPERATIONS

Table of Contents

CHAPTER ONE

INTRODUCTION

Cancer: the word conjures up images of a fatal disease with no cure and a horrible outcome. Those people who were in the prime of their lives wither away and die in a matter of few months. However, this is not true for many cancers today. Today there is hope. With early detection and modern therapy, most people can expect long fulfilling lives even from those diseases that were considered untreatable just a few decades ago. Unfortunately, for those people suffering from what is known as high grade gliomas, that hope does not yet exist. To this date, there is no accepted cure to this fatal disease which afflicts over 300,000 people annually in the world.[1] This disease which is the number two cancer killer of young children, only behind leukemia, stands undaunted by the best that modern medicine can offer. In addition, early detection of this fatal cancer is difficult due to its lack of and variation of symptoms in its early states.

The problems faced by those physicians treating high grade gliomas are formidable. The disease has a uniformly dismal outcome with average survival after therapy lasting a mere 4

to 6 months. The disease does not seem affected by dose/time/volume factors in radiotherapy, the use of hyperbaric oxygen, chemical radio-sensitizers, adjuvant chemotherapy, immunotherapy, and particle beam therapy. Even with the best modern multi-modality therapy, the 5-year survival rate for this disease is less than 4%.[1] However, recent work by Dr. Hiroshi Hatanaka in Japan with a new form of cancer therapy, boron neutron capture therapy (BNCT), holds the promise of a potential cure for this otherwise fatal disease.

Although Locher theorized as early as 1936 that boron used with slow neutron irradiation may be used for tumor therapy, it wasn't until 1951, that a neutron beam with enough intensity became available.[2] In 1951, Sweet at the Massachusetts General Hospital (MGH) and Farr at the Brookhaven National Laboratory with their co-workers treated a 51-year old woman with fatal grade IV-glioma, also known as glioblastoma multiforme, with this revolutionary new process.[3] By bombarding the non-radioactive boron-10 nucleus, that had been injected into her tumor, with slow neutrons they were able to create mini-nuclear fission reactions in her body. Boron-10 nuclei react with the slow neutrons to produce an alpha particle and a lithium ion with 2.3 MeV of kinetic energy. The immense energy produced by this reaction is dissipated within a few microns and thus in theory, can kill the tumor cells if the boron-10 fission occurs in or near a tumor cell.

The first BNCT patient was not cured by this therapy. Nor were dozens of patients that followed her, first at BNL, and later at the Massachusetts Institute of Technology (MIT). The neutron beam that was being used for the therapy at that time was partially responsible for this dismal outcome. The neutron beams at both BNL and MIT were nearly thermal in energy. This meant that the highest neutron flux were delivered at the surface after which the intensity dropped rapidly with depth. The outcome was that patients suffered tremendous radiation scalp damage and poor tumor kill at depth in tissue resulting in their deaths. However, the trials at MIT weren't all for naught. Although all eighteen patients

treated at MIT also died, in two patients, their tumors were completely destroyed. For the first time, it was shown that gliomas can be destroyed by using high LET radiation.

Although clinical trials of BNCT were discontinued in the U.S. after 1961, the BNCT procedure was carried on in Japan by a former associate of Sweet, Dr. H. Hatanaka. By improving the therapy with several new innovations, Hatanaka has shown some remarkable successes for patients with high grade gliomas. His improvements include: 1) open craniotomy and complete debulking of the tumor prior to therapy to increase neutron penetration, 2) injection of adrenocorticosteroid to suppress radiation damage of healthy blood vessels, and 3) reduced radiation doses to limit injury to the healthy brain.[4] Five-year survival rates for those patients with shallow lying tumors are as high as 58%. Overall, for Hatanaka's BNCT patients, the 5-year survival rate is an impressive 19%.

Hatanaka's impressive results have revitalized interest in BNCT, not only in the U.S. but in the rest of the world. The extensive experience gained during the 20 years that Hatanaka has been treating patients using BNCT points out the need for several improvements in the next generation of neutron beams. The significant difference in the survival rates for the shallow tumors versus the deep lying tumors suggest a need for a neutron beam with greater penetration in tissue, i.e. an epithermal neutron beam. The complications that can result from open craniotomies during irradiation suggest a need for a neutron beam which can eliminate this difficult procedure. Clinical results and improved understanding of glioblastoma physiology also seem to indicate a need for a beam large enough to treat the entire brain.

To summarize, the characteristics of neutron beams required for improved boron neutron capture therapy are: 1) high peak to surface ratio of thermal neutron flux to eliminate the need for an open craniotomy with the peak flux located at greater than 1 cm depth (approximate thickness of the scalp and skull); 2) the ability to treat tumors as deep as the

mid-line of the brain; and 3) a large beam area to permit treatment of the entire brain if necessary.

At the MIT Research Reactor, an effort has been underway for the past three years to develop an epithermal neutron beam which would meet these three criteria. Using simple hand calculations, extensive Monte Carlo computer calculations, along with experimental measurements, over 100 filter configurations have been designed for the medical therapy beam at MITR-II. Based on the calculations, over 40 filters were designed, built, and installed in the medical therapy beam and their characteristics were experimentally measured using a combination of gold foils and paired ion chambers in head phantoms. These analytical and experimental efforts have provided a clinically useful epithermal neutron beam.

In the following chapters, there will be a brief discussion of the nature of gliomas followed by a summary of the conventional treatment protocols for this disease and their outcome. This will be followed by a brief history of boron neutron capture therapy as well as a discussion of the effort at the MITR-II to develop a clinically useful epithermal neutron beam. The results from complete dose vs. depth characterizations of such epithermal neutron beams in both a cylindrical water phantom and the ellipsoidal water phantom will be also presented. In addition, the dosimetry techniques and phantoms used for the beam development work will be discussed. Finally, a selected summary of calculation and experimental results from the epithermal neutron beam development at MITR-II will be presented in tabular, graphical, and database formats.

REFERENCES

1. K. Jellinger, "Present limits of conventional treatment for malignant brain tumors," Boron-neutron capture therapy for tumors, Nishimura Co., Niigita, Japan, 1986.

2. G. Locher, "Biological effects and therapeutic possibilities of neutrons," American *Journal of Roentgenology*, 1936, 36: 1-13.

3. L. Farr, W. Sweet, J. Robertson, C. Foster, H. Locksley, D. Sutherland, M. Mendelson, and E. Stickley, "Neutron capture therapy with boron in the treatment of glioblastoma multiforme," *American Journal of Roentgenology*, 1954, 71: 279-291.

4. H. Hatanaka, and K. Sano, "A revised boron-neutron capture therapy for malignant brain tumours, I. Experience on terminally ill patients after Co-60 radiotherapy," *Journal of Neurology*, 1973, 204: 309-332.

CHAPTER TWO

MALIGNANT BRAIN TUMORS

2.1 INTRODUCTION

Malignant brain tumors result in over 300,000 deaths each year in the world. According to recent data collected in 1974, in the United States over 17,000 people were diagnosed with having primary brain tumors annually and over 17,400 people, with secondary intracranial neoplasms (ICN). Of these, more than half of the people diagnosed with primary brain tumor die each year from central nervous system (CNS) failures.[1] Among people dying from solid tumors, brain metastases are found in over 25% of the cases and are often the cause of deaths. In addition, among children brain tumors are second only to leukemia in frequency and will kill over 1,600 children and young people annually.[2]

Brain tumor ranks ninth in terms of terminal cancers reported in the U.S. as shown in table 2-1.[3] However in terms of mortality per given incidence ratio, brain tumor ranks second only to lung cancer in its deadliness. Like many terminal cancers, there is no cure and life expectancy after diagnosis is short, ranging from 5 to 6 months for primary tumors and

about 4 months for the brain metastases. In addition, early detection of these tumors is very difficult and the symptoms during the early stages of the disease are slight or nonexistent. Conventional therapy of either surgery or radiation therapy, or both, may extend the survival of the patients by 3 to 6 months for those patients with higher grade tumors.

Table 2-1: Average annual incidence and mortality rate and percentage distribution of cases and deaths, by primary site, both sexes, and all races in the United States from 1973 to 1977†

Cancer	Rates (per 100,000) Incidence	Mortality	% Cases	Deaths
Digestive system	78.9	46.1	23.7	28.5
Respiratory system	52.6	39.7	15.8	22.9
Breast	46.7	15.1	14.0	9.2
Female genital system	31.7	10.4	9.6	5.9
Male genital system	30.4	9.2	9.1	5.6
Urinary system	22.4	7.8	6.7	4.5
Lymphomas	12.0	6.0	3.7	3.6
Buccal cavity and pharynx	11.2	3.7	3.4	2.3
Leukemias	9.8	6.7	3.0	4.1
Skin	6.6	2.4	2.0	1.3
Brain and other nervous system	5.3	3.9	1.6	2.3
Endocrine system	4.4	0.6	1.4	0.4
Other	19.5	14.9	5.8	8.9
Total	331.5	166.5	100.0	100.0

† data are from National Cancer Institute

The tumors show biphasic distribution in age, with childhood peak (ages 5 to 9) and adult peak (ages 50 to 55). The most common types of childhood brain tumors are medulloblastoma, followed closely by astrocytoma. For adults, the tumors tend to be much more malignant, with over half the cases being high grade glioblastoma.[4]

The higher fatality rate for brain tumors may be partially due to the fact that there are many unique properties to the brain that pose additional difficulties to conventional cancer therapy. Because the brain is enclosed in a closed cavity and many areas are vital to survival, benign forms of tumors that may pose no danger elsewhere in the body can be

fatal when occurring in the brain. In addition, the brain is protected by the blood-brain-barrier (BBB). This tight regulation of transport across blood capillaries serves to restrict most chemotherapeutic agents and may contribute to limiting the exposure of brain tumor antigens to the immune system.

In general, brain tumors can be divided into two classes: 1) primary tumors originating in the brain, and 2) brain metastases arising from tumors elsewhere in the body. Primary brain tumors are gliomas, astrocytomas, adenomas, ependymomas, medulloblastomas, oligodendrogliomas, and others, and rarely metastasize outside of the neural cavity. Brain metastases are mainly from melanomas, lung, breast, kidney, nasopharyngeal, and thyroid cancers.

2.2 PRIMARY BRAIN TUMORS

Primary brain tumors are mainly composed of four major types: gliomas or astrocytomas, meningiomas, ependymomas, adenomas. Of these, it is the gliomas that are the primary target for BNCT. Grade I and II gliomas are often referred to as astrocytomas and are usually benign. More malignant grade III and IV gliomas are referred to as glioblastoma multiforme and form the majority of primary brain tumors in adults. Sometimes, grade III gliomas are also referred to as astrocytomas with only grade IV gliomas being referred to as glioblastoma multiforme.

Tables 2-2 and 2-3 summarize the incidence rate and survival rates for these tumors. There is tremendous variation in the data. This has a lot to do with the difficulty in correctly diagnosing the tumor. In addition, Walker notes that statistics on tumors vary from center to center, depending on the capability and interest of the medical staff.[5] The overall value given is a summation of several series from different medical centers. However what is clear is that glioblastoma multiforme is by far the most common brain tumor in adults.

Unfortunately glioblastoma is also one of the most fatal cancers, with median survival after therapy of 4.5 months.

Table 2-2: Relative frequency of the common primary brain tumors as reported by various authors; sampling population is shown for each series.

Tumor	Salcman[4] Adults n = 2119 (%)	Walker[5] Children n = 948 (%)	Walker[5] Adults n = 948 (%)	Walker[5] Overall n = 17,580 (%)	Jellinger[1] Overall n = 17,000 (%)
Glioblastoma multiforme	52.1	10	47	23	58*
Astrocytoma	10.1	19	24	13	
Meningioma	18.4	–	–	16	20
Ependymoma	1.3	16	6	1.8	–
Adenoma	5.7	–	–	8.2	14
Medulloblastoma	1.3	20	1	1.5	–
Oligodendroglioma	1.0	0	3	1.6	–
Other	17.1	35	19	34.9	8

* The fraction includes all gliomas including astrocytomas.

According to table 2-3, most fatalities from brain tumors come from high-grade gliomas and ependymoma. However, ependymoma incidence is quite low, as shown in table 2-2. Therefore, malignant primary brain tumors are basically composed of grade III and IV gliomas. In fact, of all the people that die of primary brain tumors each year, over 75% die from high-grade gliomas.

Table 2-3: Survival rates for various brain tumors from time of diagnosis according to Salcman[4]

Tumor	% surviving 1 year	% surviving 2 year	% surviving 5 year
Astrocytoma grade I	90	87	76
Astrocytoma grade II	85	75	58
Astrocytoma grade III	39	18	6
Glioblastoma Multiforme	32	11	0
Ependymoma	50	47	25
Meningioma	100	95	90
Medulloblastoma	–	70	56

2.2.1 Gliomas

Gliomas are cancers of the glial cells and are often graded into 4 groups based on histological observations. Grade I gliomas, or astrocytoma grade I, are difficult to detect with the unaided eye. Under the microscope, they are characterized by increased numbers of normal looking astrocytes infiltrating into the surrounding area without any nuclear dimorphism. Grade II astrocytoma differs from grade I in that the density of the astrocytes is increased and there is now some evidence of abnormality in cell structure. Grade III gliomas are malignant, and under the microscope the abnormalities are quite plain. The cells often have scanty cytoplasm and the nuclei are hyperchromatic. Giant cells with multinuclei are also often present. There may also be areas of necrosis and hemorrhage. All of these features are also characteristic of grade IV gliomas, also called glioblastoma multiforme. In addition, glioblastoma multiforme is characterized by an increased number of mitotic figures, atypical nuclei, and cellular pleomorphism (multiple structure). There is also extensive capillary proliferation with a multitude of color and texture. Grade I and II gliomas are considered benign and, if detected early, can be treated with good results using conventional multi-modality therapy. Malignant variants, grade III and IV gliomas, are almost impossible to cure using conventional therapy and are the main focus of BNCT.

There is very little data on the cause of gliomas. Unlike many other cancers, there is apparently no link between increased risk of contracting glioma and the various known carcinogens. Neither is there a link with genetic variables or socioeconomic variables. It appears that glioma affects both white and non-white as well as rich and poor alike. Some researchers believe that this is due to the unique nature of the brain, such as the BBB and the lack of a common lymphatic system. Indeed the gliomas differ from other cancers in that they almost never metastasize to other parts of the body even in the most malignant stages.

2.2.2 Symptoms

Patients with gliomas often have no symptoms until the tumor has progressed well into its malignant stage. Because, the brain lacks specific nervous feedback within itself, the tumor is often detected through secondary effects. Most symptoms are site-specific to the tumor and do not depend on the histological grade of the tumor. The tumor growth causes increased pressure on various areas of the brain, which results in partial paralysis or mood changes. Because the brain can adapt relatively well to slow growing tumors, an increase in cranial pressure is often absent in those patients with lower grade tumors.

Depending on where the tumor is located, the symptoms differ widely. For example, disturbance in memory and judgement indicate tumors in frontal and temporal lobes. Weakening of sight usually indicates tumors in occipital lobes. Table 2-4 summarizes the various symptoms associated with tumors occurring in different parts of the brain, along with their relative frequency. It should be pointed out that these symptoms can also be produced by neurological effects other than brain tumors. For example, rapid onset of symptoms often indicates vascular damage in specific areas of the brain rather than brain tumors. Symptoms from brain tumors tend to be far slower in their progression.

Some of the early symptoms of brain tumor in adults are headaches, weakness, seizures,

Table 2-4 Typical symptoms of site-specific brain tumors with their relative frequency of occurrence

Symptoms	Location	%
Disturbance in memory and judgement	Frontal/temporal lobes	30~60
Disturbance of personality	Frontal lobes	30
Contralateral weakness and numbness	Frontoparietal cortex	11
Contralateral visual fields deficit	Occipital lobes	5
Ipsilateral incoordination of limbs	Cerebellar hemisphere	--
Incoordination of gait	Cerebellar vermis	--

personality changes, and onset of epilepsy. The headaches often appear to be most severe in the morning. This is thought to be caused by increased retention of carbon dioxide during sleep. Elevation of carbon dioxide concentration in blood can result in engorgement of cranial blood vessels, resulting in elevated intracranial pressure (ICP). It is this effect, coupled with the growing tumors, that causes these morning headaches, which are described as being of the all-over variety.

2.2.3 Clinical diagnosis

Once these early symptoms are detected, clinical diagnosis must be made to ascertain the nature of the symptoms. In the past, electroencephalograms (EEG) or angiograms were used to diagnose brain tumors. Brain scans using radioactive isotopes of mercury (^{197}Hg and ^{202}Hg), iodine (^{131}I), and technetium (^{99m}Tc) were also used by physicians during the early clinical trials of BNCT. These all had accuracies of between 70% and 85% if used correctly. However, with the advent of the modern computerized tomography machines, CT has basically replaced all other means of clinical diagnosis.

The accuracy of CT scans, used both in the unenhanced mode as well as with contrast agents, is better than 95%. By the size, shape, location of the tumor, extent of edema surrounding the tumor, and the degree of contrast enhancement, a radiologist can even determine the specific histology of the tumor. As good as the CT scan is now, it is currently being supplemented by nuclear magnetic resonance imaging (MRI). Although its spatial resolution is not as good as the CT scan, it is able to image metabolic parameters as well as the spatial density, this is better in some instances for imaging viable tumors.

Once the brain tumor is diagnosed using a CT scan and/or a MRI scan, microsurgery or CT-guided stereotatic biopsy may be used to obtain tumor samples to determine the precise

tumor histology. However, often the histological sample is obtained during the actual surgery for tumor resection as part of an overall multi-modality treatment protocol.

Table 2-5: Performance status or Karnofsky scale

Status	Criteria for performance status
100	Normal; no complaints; no evidence of disease
90	Able to carry on normal activity; minor signs or symptoms of disease
80	Normal activity with effort; some signs or symptoms of disease
70	Cares for self; unable to carry on normal activity or to do active work
60	Requires occasional care for most needs
50	Requires considerable assistance and frequent medical care
40	Disabled; requires special care and assistance
30	Severely disabled; hospitalization is indicated although death is not imminent
20	Very sick; hospitalization necessary; active supportive treatment is necessary
10	Moribund, fatal processes progressing rapidly
0	Dead

Another important diagnostic tool in judging prognosis of brain tumor patients is the Karnofsky scale shown in table 2-5. This scale judges the performance status of a given individual and is a useful tool in determining the extent of the tumor progression and potential survival after therapy. It has been shown that patients with a performance status under 50 have a significantly worse prognosis than those with a higher Karnofsky scale.

2.2.4 Conventional therapy

Conventional therapy for high-grade gliomas consists of aggressive surgical resection of the tumor followed by radiotherapy and/or chemotherapy. The amount of tumor that can be safely removed depends largely on its location, not only in terms of accessibility, but also on the importance of the surrounding areas of brain for normal human function. For example, tumor near the dominant speech areas may only be subjected to biopsy, whereas tumors arising in non-critical areas of the brain may be extensively resected.

Radiation therapy is used for most patients suffering from primary brain tumors. For glioma patients, the standard radiotherapy regimen includes 45 to 60 Gy of photon to the entire brain delivered in approximately 2 to 3 Gy daily fractions. This is usually followed by an additional 20 Gy photon boost to the tumor site. In recent years, an additional 100 to 200 Gy photons have been given to the tumor bed using radioactive iridium or gold implants. Even with such large doses, standard photon therapy does not seem to appreciably lengthen the survival of those patients with glioblastoma multiforme.

Chemotherapy is often given in conjunction with the surgery and radiotherapy. Corticosteroid is used prior to surgery to control cerebral edema resulting from tumor growth and is often a good indicator as to how the patient will respond to the surgical procedure. Following the operation and during the radiotherapy, corticosteroids help control swelling associated with the trauma of surgical resection and radiation.

A number of other drugs have been tried for brain tumors. However the results have been disappointing. Drugs such as bleomycine, methotrexate, and mithramycine, which are widely used in the treatment of other tumors, have been shown to be ineffective for brain tumors. The only drugs that seem to have positive tumor control have been N,N'-bis(2-chloroethyl)-N-nitrosourea (BCNU) and its variant CCNU. This therapy is usually initiated at the conclusion of radiotherapy. The patient is given an initial dose of 100 mg/sq m/day for 3 days and this is repeated every 8 weeks until a total dose of 1500 to 2000 mg/sq m is achieved. The patients that have been on this therapy seem to show slightly better short term survival rates than those on radiotherapy alone.

Figure 2-1 illustrates the survival rate of glioblastoma patients treated with surgery alone and those treated with surgery plus radiotherapy and/or chemotherapy. This collection of studies by Salcman shows that although short term survival (< 1 year) is improved by the

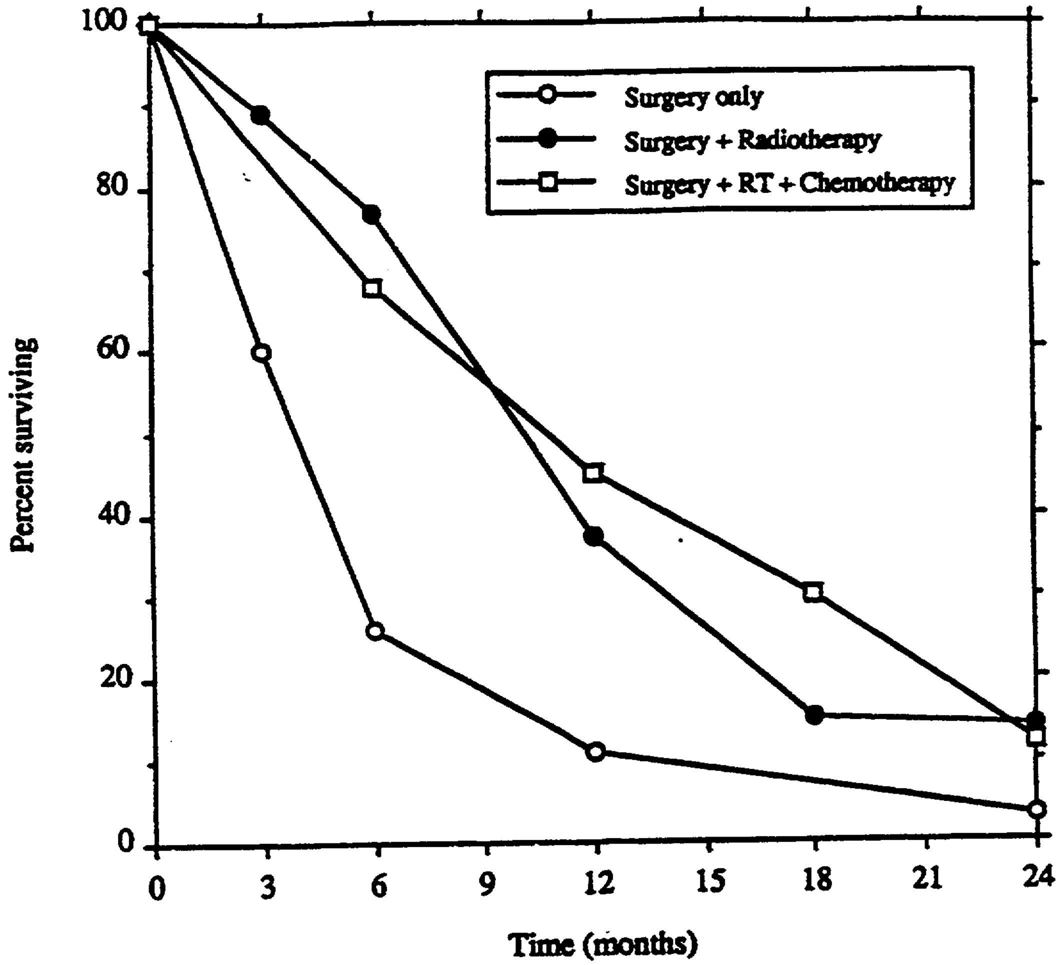


Figure 2-1: Comparison of survival rate for glioblastoma patients treated using surgery alone, surgery plus radiotherapy, and surgery plus radiotherapy and chemotherapy

(Redrawn from Salcman, 1980)

additional treatments, the survival rates for periods beyond 2 years converge regardless of the nature of the therapy.

Another study by Jellinger compared the efficacy of various chemotherapy and radiotherapy protocols with surgery alone and multimodality therapy on grade III and IV glioblastoma patients. Table 2-6 outlines these therapeutic protocols along with the number of patients in the study group and their mean survival rate. Figure 2-2 shows the survival rates for these various treatment protocols. Only the multimodality group shows any patients with a 5-year survival rate. At 4%, even this is somewhat disappointing.

If only the grade IV gliomas are counted, the results are even more dismal, as shown in figure 2-3. With surgery alone, the 1 year survival rate is only 3%. With surgery and

Table 2-6: Description of treatment protocols for patients with grade III and IV gliomas used in Jellinger's study along with their mean survival rate post-op

Clinical protocol	# Patients			Mean Survival (months)		
Tumor grade:	3	4	3+4	3	4	3+4
Surgery only	30	37	67	10.7	4.2	7.2
BCNU monotherapy: CCNU 100 mg/sq m post-op every 6 weeks	--	--	16	--	--	7.7
Radiotherapy: 40 to 66 Gy photon over 7 weeks	37	31	68	15.4	8.6	12.3
Polychemotherapy (ISRAEL): in 7 day cycles 6-mercaptopurine (500 mg p.o.) daily Cyclophosphamide (500 mg iv) day 1, 3, 5 5-fluorouracil (250 mg iv) day 2, 4, 6 Methotrexate (MTV) (5 mg iv) day 1, 4 Vinblastine (5 mg iv) day 7	--	--	15	--	--	13.8
COMP protocol (HEISS): in 15 day cycles CCNU (100 mg/sq m) day 1 Procabazine (100 mg/sq m iv) day 2-13 Methotrexate (10 mg/sq m iv) day 3, 7, 10 Vincristine (1.4 mg/sq m iv) day 1, 8	22	21	43	16.8	9.4	13.2
Combined radiotherapy and COMP therapy: 60 Gy photon with COMP protocol	41	60	101	32.5	14.8	22.2

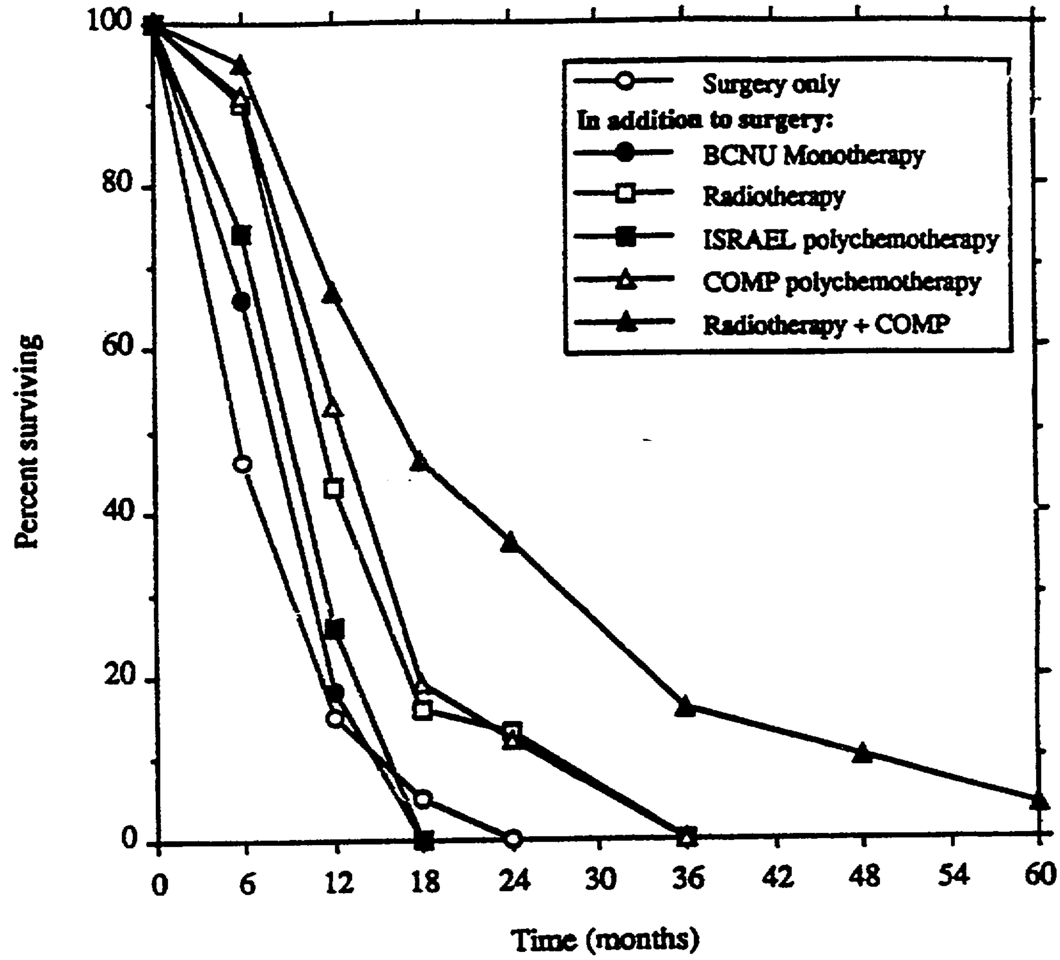


Figure 2-2: Survival rates for grade III and IV glioblastoma patients treated using various clinical protocols

(From Jellinger, 1986)

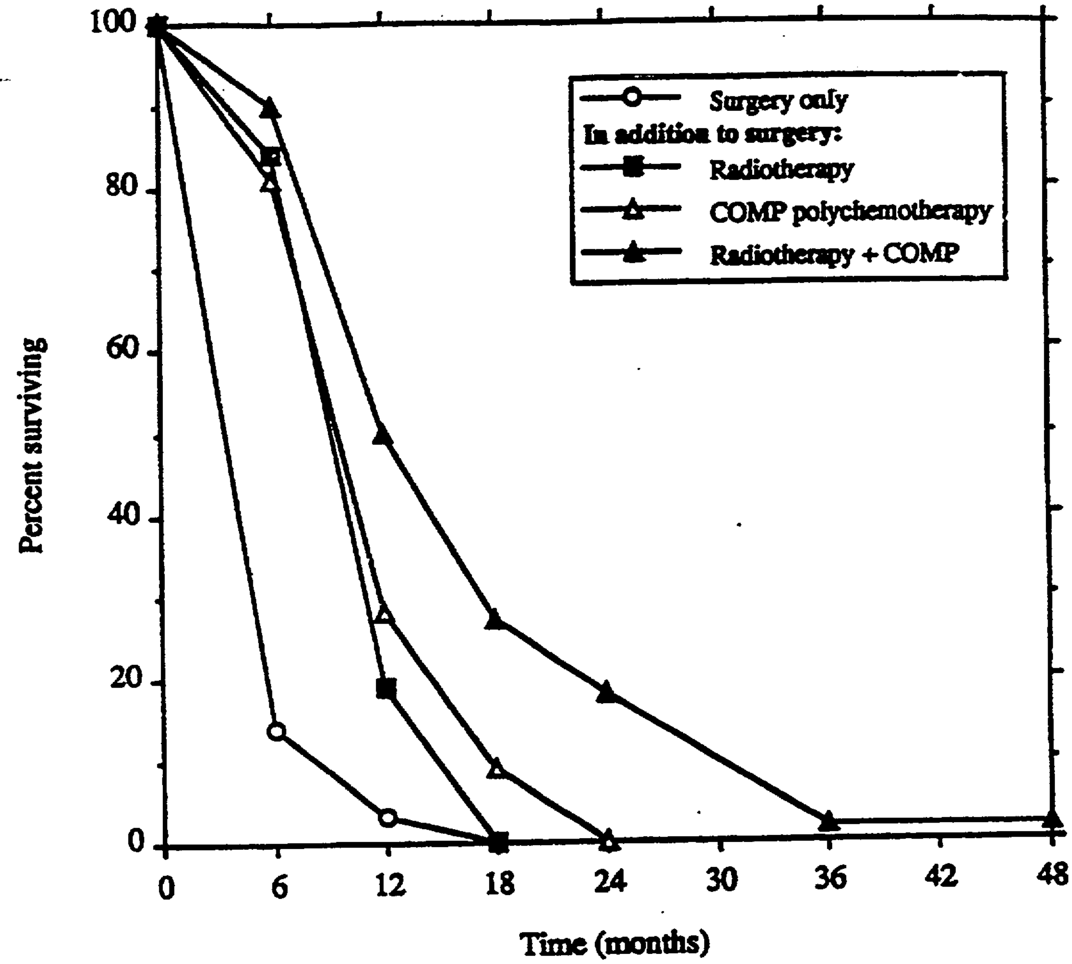


Figure 2-3: Survival rates for grade IV glioblastoma multiforme patients treated using various clinical protocols

(From Jellinger, 1986)

radiotherapy, the 1 year survival rate increases to 19%, but there are no survivors past 18 months post-op. With polychemotherapy in conjunction with surgery, but without radiotherapy, the 1 year survival rate is still greater, at 28%, and there is even a 9% survival rate for 18 months. However, there is still no survivor past 2 years with polychemotherapy. The best results were obtained with multimodality therapy, including surgery, radiotherapy, and chemotherapy. With this therapy, the 1 year survival rate is 50% and the 2 year survival rate is 18%.

2.3 BRAIN METASTASES

Another major class of intracranial neoplasms is the secondary brain tumors that has metastasized from other cancerous regions in the body. Among the major tumors in the body, brain metastases from melanoma are by far the greatest. More than 75% of the patients with malignant melanoma, also show signs of brain metastases of melanoma. The other major cancer groups, such as lung, breast, kidneys, etc., show less than 25% to 50% incidence of brain metastases.

Often when a tumor has metastasized to the intracranial cavity, this indicates a primary tumor that is well advanced into its malignancy. The outcome for such patients is uniformly hopeless, with median survival after the discovery of metastases of less than 4 to 6 months. Oftentimes such metastases are only discovered during autopsy after the patient has succumbed to the primary tumor.

REFERENCES

1. K. Jellinger, "Present limits of conventional treatment for malignant brain tumors," Boron-neutron capture therapy for tumors, Nishimura Co., Niigita, Japan, 1986.

2. H. Bloom, "Intracranial tumors: Response and resistance to therapeutic endeavors, 1970-1980," *International Journal of Radiation Oncology, Biology, and Physics*, 1983, 8:1083-1113.

3. A. Moosa, M. Robson, S. Schimpff ed., Comprehensive Textbook of Oncology, Williams and Wilkins, Baltimore, 1986.

4. M. Salcman, and R. Kaplan, "Chap 59: Intracranial tumors in adults," Comprehensive Textbook of Oncology, Williams and Wilkins, Baltimore, 1986, 617-629.

5. M. Walker, "Chap 20-1: Brain and peripheral nervous system tumors," Cancer Medicine, Lea and Febiger, Philadelphia, 1973, 1385-1407.

Chapter Three

APPLICABILITY OF BORON NEUTRON CAPTURE THERAPY

3.1 INTRODUCTION

The basic principles of boron neutron capture therapy (BNCT) have been around since Locher first described them in his discussion of possible medical uses of neutrons in 1936.[1] Boron, having a high affinity (cross section) for thermal neutrons, will absorb a thermal neutron and fission into an alpha particle and a lithium ion releasing 2.78 MeV of energy. This is shown schematically in figure 3-1. About 93% of the time, 0.48 MeV of this reaction energy is released as a single gamma ray of equivalent energy. The rest of the energy released in the reaction goes into the kinetic energy of the recoiling products, an alpha particle and a lithium nucleus which move in opposite directions to conserve momentum. Because these are heavy, charged particles, they rapidly lose their energy through ionization in tissue or other material. It is these secondary ionization that causes intracellular damage in tissue. Gabel et al. have calculated the rate of energy loss to the tissue from the BNCT reaction, and the results are shown in figure 3-2.[2] As shown in the figure, both particles dissipate most of their energies within 10 microns. Ten

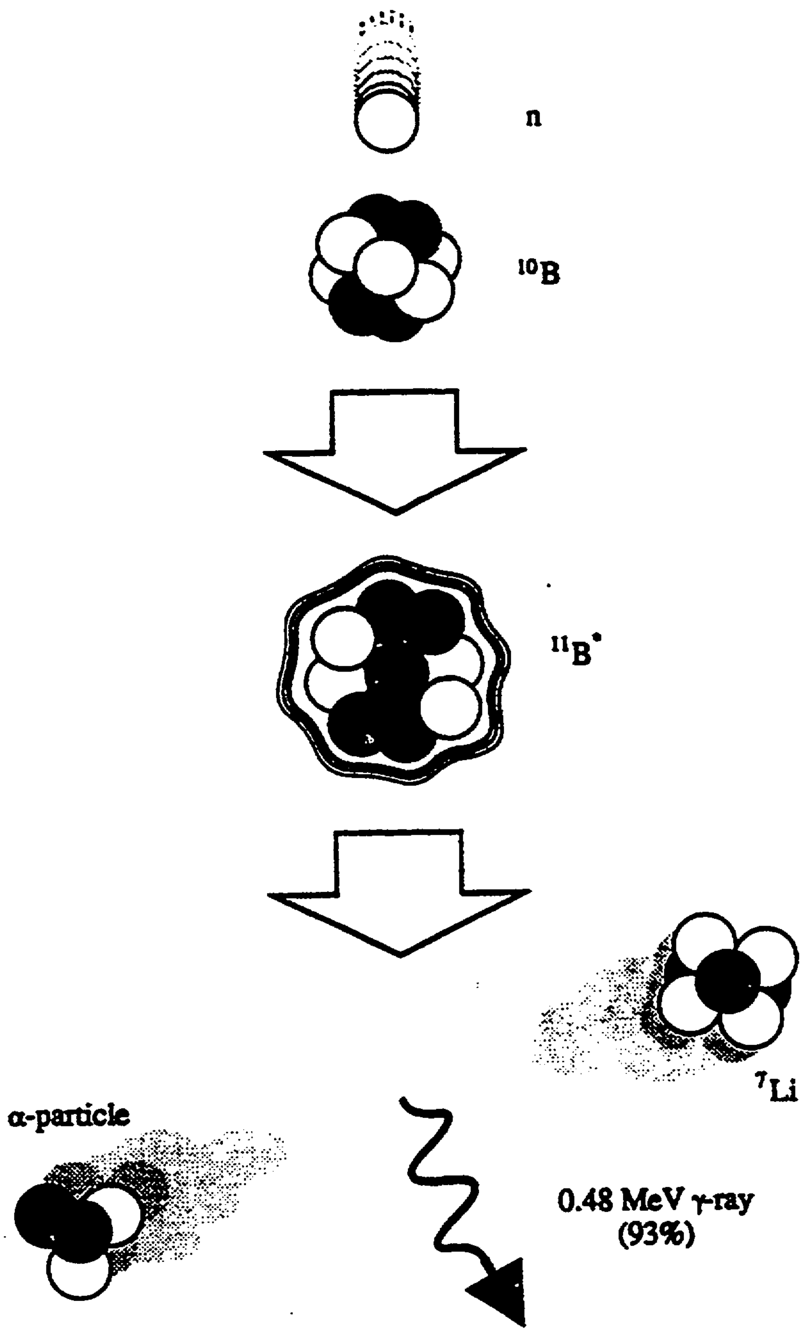


Figure 3-1: Graphic schematic of the boron neutron capture reaction. Slow neutron is captured by the boron-10 nucleus forming an unstable boron-11 nucleus which promptly fission into an α-particle and a lithium ion with 2.78 MeV of excess energy. Gamma ray with 0.48 MeV energy is also emitted 93% of the time.

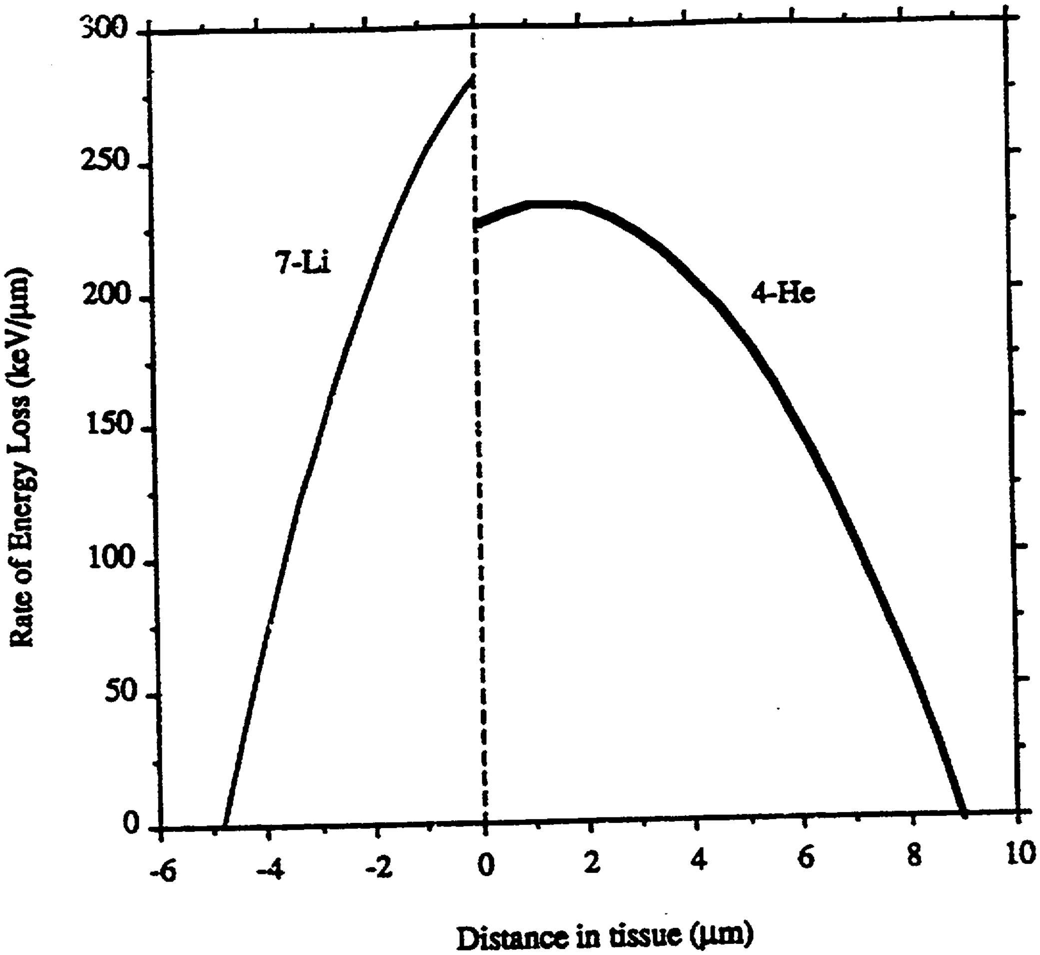


Figure 3-2: Rate of energy loss for the two particles generated in the BNCT reaction [2]

microns is approximately the diameter of most cells. Therefore, if the (n,α) reaction occurs within the cell boundaries, most of its energy will be dissipated within the cell. This is important because the dose is then restricted only to those cells containing boron and will not affect neighboring healthy cells.

Boron neutron capture therapy is in essence a combination of chemotherapy and radiotherapy. Because it requires that both the boron and the neutron be present to kill the tumor, it can be, in principle, much safer and effective then either chemotherapy or radiotherapy alone. With chemotherapy, one relies on massive concentrations of tumor-seeking drugs to kill the tumor. Unfortunately, most of these drugs also have adverse effects on the various non-tumorous organs of the body such as liver or kidneys. This puts inherent restrictions on the amount of drug that can be tolerated, thus reducing the chances for a complete cure.

Radiotherapy on the other hand, can be effective on tumors provided that a tumor is localized and has not metastasized to other organs of the body. Once the tumor has spread throughout the body or the organ, the selective advantage of the radiotherapy is lost. Because one can no longer focus the radiation to specific tumor sites, the radiation delivers the same amount of dose to healthy tissue as to tumor. Furthermore, the conventional radiotherapy typically uses x-rays or gamma rays, these have ranges on the order of tens of centimeters in tissue. Therefore, they are far less specific than the ions resulting from the BNCT reaction, which lose all their energy within 10 μm of their origin.

With BNCT, one can be far more specific, because only the cells that have incorporated boron will be affected by the (n,α) reactions induced by the neutron field. Its only when these two ingredients, boron-10 in tumor and neutron induced (n,α) reactions are present, that the lethal effects are produced.

However, it wasn't until the 1950's that Locher's ideas could be used in therapy. Prior to this, there was no neutron source that was intense enough to be used as a therapeutic tool. In 1950, the large 30 MW_t graphite-moderated air-cooled reactor (BGRR) became available at Brookhaven National Laboratory (BNL). For the first time, neutron fluxes greater than 10^8 n/cm^2 sec was available for medical research. BNCT, with its unique potential, was initiated almost immediately at the BGRR by a group from BNL and the Massachusetts General Hospital (MGH) and later at the Massachusetts Institute of Technology Research Reactor (MITR) by a group from MIT and MGH. These experiences were uniformly dismal, yielding only 5.7 months of mean survival time after therapy.[3] Most of the patients treated during this time showed recurrence of tumors and in some cases necrosis of the normal brain and scalp. Despite such failures, in 1964, a Japanese post-doctoral scientist, Dr. Hiroshi Hatanaka, working at Massachusetts General Hospital became interested in BNCT. After surmounting various institutional difficulties, Hatanaka started treating his patients using BNCT with thermal neutron beams and improved boron delivery agents upon his return to Japan in 1968. As of March 1989, he had treated 98 patients using BNCT; 49 of which were affected with grade III and grade IV gliomas. In some cases, his therapy has achieved a 5-year survival rate of over 50%. In this chapter, the clinical trials of BNCT by the BNL/MGH group, the MIT/MGH group, and of Hatanaka, using thermal neutron beams, will be briefly reviewed.

?.2 CLINICAL TRIALS AT BROOKHAVEN NATIONAL LABORATORY

In 1951, based on a report by Conger and Giles at Oak Ridge of the efficacy of slow neutrons in producing a large amount of radiation damage to lily bulbs as a direct result of trace amounts of boron in them, Sweet and Javid at MGH decided to use this phenomenon to treat primary brain tumors.[4] Because the normal brain is protected by the blood brain

[Missing pages refer to clinical trials conducted at the Brookhaven National Laboratory in the 1950s]

elsewhere in the brain. In many of the pathological examinations of these patients, very large tumors, often encompassing the entire half of the brain, were found.

The third area in which they needed improvement was in finding a better boronated agent. The borax which they were using relied only on the BBB to achieve a selective concentration in tumor. The tumor to normal brain ratio varied widely over individuals and therefore no reliable prediction could be made of the dosage to the various tissues in the brain. In addition, some damage was found in the blood vessels of the brain; no doubt due to the high concentration of boron that remained in the blood. Finally according to Farr et al, the borax in the amount used for the therapy appears to have toxic effects.[6] The intake of borax was followed by retching and often by the evacuation of bladder and bowels. Respiratory arrest was noted in one patient and poor color was observed in most of the patients following the injection.

During the two year's span from February of 1951 to February of 1953, the group at BNL, along with the group from MGH, used BNCT to treat 10 patients at the 30 MW_t Brookhaven graphite air-cooled reactor. Although all of the patients died shortly after therapy, many important lessons had been learned. The possibility of using NCT to treat malignant brain tumors was shown. About half the patients showed remarkable, albeit brief, recovery after the therapy. It was shown that no serious complications occurred directly from the therapy. Perhaps most importantly, this pioneering work laid the ground work for further BNCT trials of malignant CNS tumors which cannot be successfully treated with conventional modalities.

3.3 CLINICAL TRIALS AT THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY RESEARCH REACTOR

Ten years following the initiation of NCT at BNL, Sweet and his group from MGH along

with the group at MIT led by Brownell conducted the fifth major clinical trial of BNCT at the Massachusetts Institute of Technology Research Reactor. The MITR-I, unlike the BGRR that was used for the clinical trials at BNL, was heavy water moderated and cooled with graphite reflectors outside the core tank. Running at 2 MW_t power, MITR-I could provide a thermal neutron flux of > 10^{10} n/cm2 sec at its medical beam port. This was almost 30 times the available flux of the BGRR, running at 10 times the power level. In addition, the MITR-I was built with BNCT in mind and had a complete operating room built into the medical therapy facility. It is essentially identical to the current MITR-II except for the reactor core and the surrounding reflector. Figures 3-5 and 3-6 show the isometric cutaway of the MITR-I and the neutron therapy beam line.

In the ten years following the first clinical trial, a number of improvements have been made to BNCT. The first was the availability of a reactor facility with a neutron flux high enough for NCT. It was found from the BNL trial, that the tumor-to-brain ratio of boron falls rapidly with time. Therefore, a facility that can deliver a therapeutic dose in ten minutes or less was sought.[9]

The second major improvement was in the boronated agent. In the first and second series of patients treated at BNL, borax was given intravenously before therapy. Because of the high concentration of boron in the skin, major necrosis occurred in the epithelial layer exposed to neutrons. Farr et al. discovered that this could be controlled if the irradiation time was kept below 10 min so that borax would not have enough time to concentrate in the epithelial layer of the skin. However, the toxicity of the borax did not allow such short time with the available BGRR facility (with the available neutron flux, ~300 ppm of ^{10}B would need to be administered to allow total therapy time of 10 minutes). Therefore, for the third series, sodium pentaborate ($Na_2B_{10}O_{16}$) was used in solution with glucose delivered by internal carotid infusion. This allowed an increase in the concentration of ^{10}B by up to 135% with no toxic effect. However even this agent did not provide the high

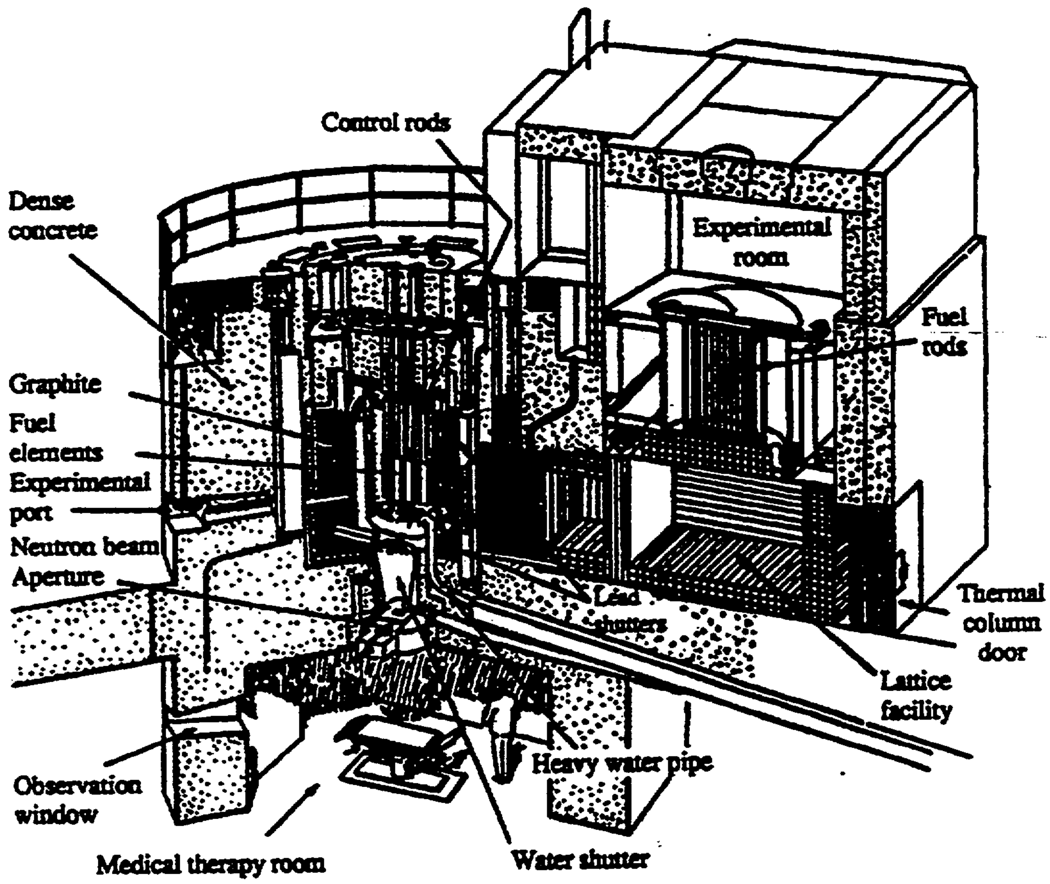


Figure 3-5: Iso-metric cut-away view of the MIT Research Reactor showing major components and experimental facilities. The reactor is MITR-I and has a different beam line then the current upgraded MITR-II.

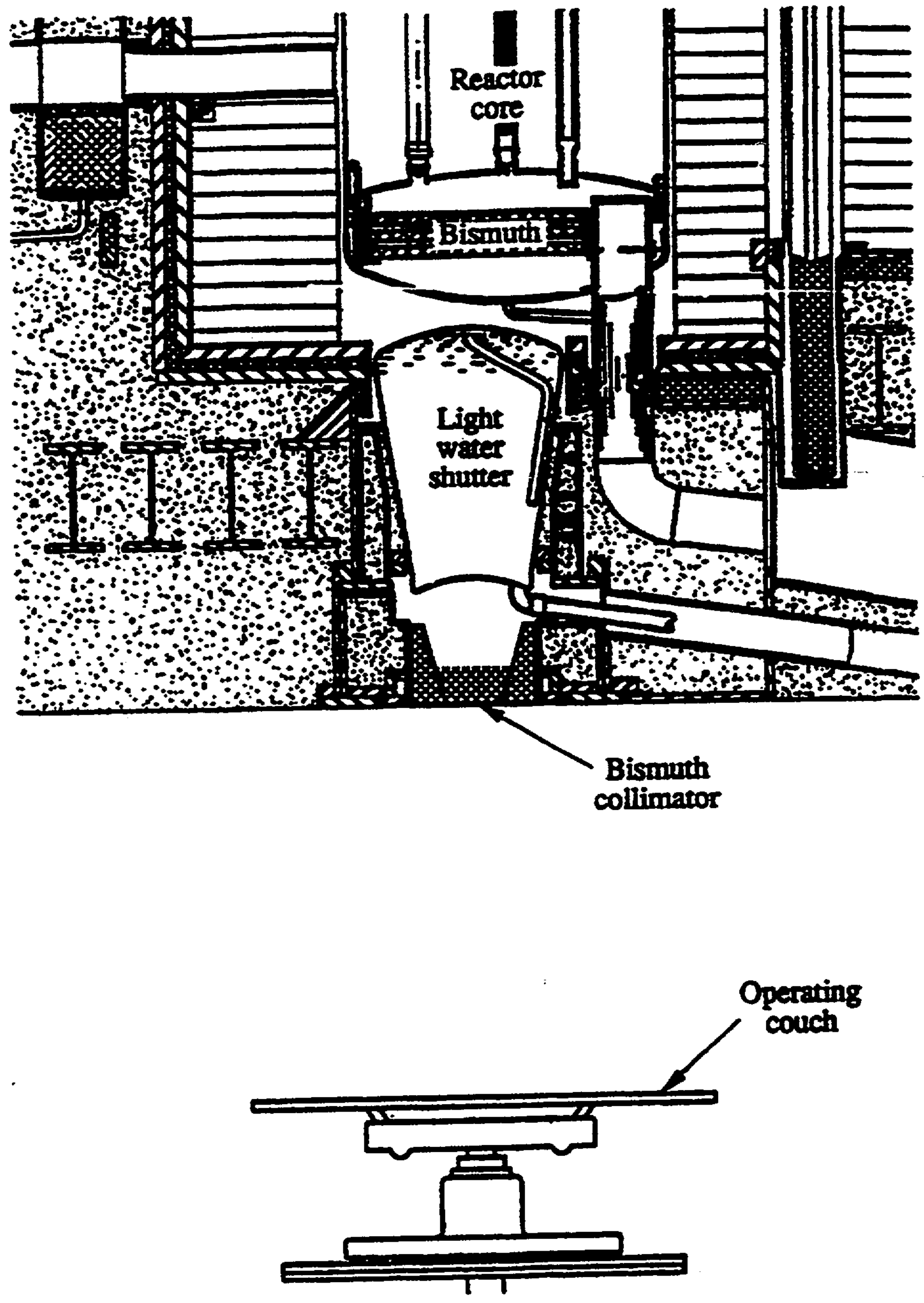


Figure 3-6: The cross sectional view of the medical therapy beam at MITR-I used for human clinical trials from 1960 to 1962.

tumor/brain ratio and low toxicity that was needed. Soloway et al. at MGH had been conducting animal and human distribution studies on a boronated compound that could be used for therapy. The compound that showed the most promise for NCT was paracarboxybenzeneboronic acid. It provided tumor/brain ratio of 5 to 7, 30 minutes after injection, and maintained this high ratio for about one hour, after which the ratio fell to 4 for the next two hours.

The third major improvement in procedure was the ability to reflect the scalp, the skull, and the dura, and expose the tumor directly to the neutron beam. This was possible because the aperture for the MITR beam was located in the ceiling of a complete aseptic operating room. The surgeon was able to perform the necessary craniotomy safely before the patient would be raised into position for the radiation therapy. Then through the viewing window, he and an anesthesiologist could monitor the patient and stop the irradiation procedure if needed.

3.3.1 First clinical series at MITR (1960-1961)

Between November of 1960 and August of 1961, 16 patients were treated at MITR with BNCT. Because it was now possible to perform craniotomies before irradiation, the procedures for NCT differed greatly from those used at BNL.

De Rougemont and Soloway demonstrated that the BBB recovers from cerebral lobectomy within 3 weeks.[11] Based on this data, NCT was administered 2 to 3 weeks following resection of the tumor. After the original surgery, the wound was closed and allowed to heal. Immediately prior to neutron therapy, the wound was reopened and reflection of the scalp, the skull, and the dura was performed to expose the tumor directly to the neutron source. This was done in the operating room built into the MITR. Because thermal neutrons are attenuated rapidly by fluid, all cerebrospinal fluid was removed from the

tumor site and replaced with an air balloon. During the course of the therapy, suction was applied to the tumor region to prevent further accumulation of fluid.

Once the craniotomy was complete, boron was given in the form of a solution of p-carboxybenzeneboronic acid through i.v. The concentration administered ranged from 15 to 30 mg ^{10}B per kg body weight. The concentration factor for boron in tumor was 1.87. The concentration factor in normal brain was about 1/4 this value, or 0.43. This meant that 30 ppm of boron injected resulted in about 56 ppm in tumor and about 13 ppm in brain. The infusion of boron took anywhere from 10 min to over an hour depending on desired concentration and patient tolerance.

Following the administration of the boron, the patient was elevated to the beam aperture by a hydraulic lift built into the floor. Once the patient was secured, everyone left the room and the built-in shutters were opened, allowing an intense beam of thermal neutrons to irradiate the open brain. The patients were irradiated for 45 min to 90 min for a total neutron fluence of 5×10^{12} to 2×10^{13} n/cm^2.

Table 3-3 summarizes the first MITR clinical trial in terms of patient's age, amount of boron, fluence given, and survival, much like table 3-1 for the BNL series. One can see that there is no apparent increase in the survival time for the patients treated at MIT vs. those treated at BNL. The average survival time after therapy is little less than 6 months.

Table 3-4 summarizes the pathological results and my estimates of the dose delivered to the tumor, normal brain and the endothelial cells of the blood capillaries. The scalp dose is not included, since with craniotomy the scalp dose is inconsequential. This time, all doses were calculated at 3 cm below the cut surface of the brain. The concentrations of boron in the tumor and the normal brain were obtained from the concentration factors described previously. The concentration of boron in the blood, based on pathological samples of

Table 3-3: Summary of clinical trials at MIT from 1960 to 1961

Patient	Sex	Age	Date of Surgery	Date of NCT	Amount of ^{10}B Given	Neutron Fluence Given	Days Survival Post NCT
No. 1 (S.E.)	F	39	Jun 20, 60	Nov 15,60	0.91 g ^{10}B (20 ppm)	1.50 E+13 n/cm^2	50 wks
No. 2 (G.R.)	F	43	Oct 6, 60	Not Irrad.			
No. 3 (G.S.)	M	14	Aug 12, 60	Nov 30, 60	1.14 g ^{10}B (20 ppm)	1.00 E+13 n/cm^2	6 wks
No. 4 (P.D.)	F	20	Dec 17, 60	Dec 30, 60	1.06 g ^{10}B (21 ppm)	2.00 E+13 n/cm^2	21 wks
No. 5 (H.C.)	F	51	Dec 7, 60	Jan 6, 61	0.69 g ^{10}B (15 ppm)	1.35 E+13 n/cm^2	8 wks
No. 6 (H.G.)	M	35	Dec 15, 60	Jan 18, 61	1.59 g ^{10}B (25 ppm)	1.10 E+13 n/cm^2	26 wks
No. 7 (J.D.)	M	43	Dec 12, 60	Jan 25, 61	1.68 g ^{10}B (30 ppm)	1.95 E+13 n/cm^2	26 wks
No. 8 (F.L.)	F	59	Dec 23, 60	Jan 31, 61	1.92 g ^{10}B (30 ppm)	2.60 E+13 n/cm^2	21 wks
No. 9 (S.W.)	M	14	Jan 28, 61	Feb 15, 61	1.35 g ^{10}B (30 ppm)	1.30 E+13 n/cm^2	39 wks
No. 10 (C.F.)	F	55	Feb 23, 61	Irr. Cancelled	0.17 g ^{10}B (3 ppm)		
No. 11 (N.L.)	F	47	Feb 27, 61	Mar 21, 61	(31 ppm)	3.30 E+13 n/cm^2	26 wks
No. 12 (C.F.)	F	55	Feb 23, 61	Apr 12, 61	1.74 g ^{10}B (31 ppm)	1.65 E+13 n/cm^2	26 wks
No. 13 (N.J.)	M	64	Mar 27, 61	Apr 18, 61	(26 ppm)	3.30 E+13 n/cm^2	21 wks
No. 14 (P.P.)	F	29	Apr 5, 61	May 3, 61	1.23 g ^{10}B (30 ppm)	2.10 E+13 n/cm^2	see No. 17
No. 15 (S.W.)	M	57	Apr 61	May 16, 61	2.33 g ^{10}B (30 ppm)	1.80 E+13 n/cm^2	35 wks
No. 16 (G.G.)	M	34	Jun 9, 61	Jun 30, 61	(30 ppm)	1.90 E+13 n/cm^2	26 wks
No. 17 (P.P.)	F	29	Jun 22, 61	Jul 19, 61	1.23 g ^{10}B (30 ppm)	2.00 E+13 n/cm^2	30 wks
No. 18 (M.J.)	M	45	Jul 28, 61	Aug 4, 61	2.09 g ^{10}B (30 ppm)	2.80 E+13 n/cm^2	13 wks
No. 19 (M.H.)	M	63	Aug 1, 61	Aug 18, 61	1.70 g ^{10}B (30 ppm)	2.35 E+13 n/cm^2	35 wks

tumor collected during operations, was found to be, on average, twice that in tumor and therefore, the dose to the capillaries was determined to be 2/3 that in the tumor.[10]

What is immediately apparent is that the doses given to the patients were enormous. Often the doses delivered to the normal brain were over 30 Gy and this was 3 cm below the surface. At the surface, the doses to the healthy tissue could have been 50 Gy or more. Likewise, the doses to the capillary wall were equally high. It is then no wonder that significant radiation damage was noted throughout the brain and the blood vessels. Although it is true that the tumors near the surface also received very high doses, because the neutrons attenuate very rapidly with depth, tumor cells at 6 or 7 cm depth only received a minor fraction of the dose near the surface. Therefore, for most of the patients, they suffered significant radiation damage, and at the same time, suffered recurrence of the tumors.

In two of the cases (G.S. and H.G.), the patients developed infections from the procedure, pointing out the risks of open craniotomy during therapy. In 5 of the 16 patients (S.E., J.D., S.W., G.G., and M.H.), there were some improvements following the therapy. The rest showed no improvement following therapy. There doesn't seem to be a correlation between dose and patient outcome. If we divide the 16 patients into two groups with one receiving 20 Gy or more to the brain at 3 cm and the other receiving less than 20 Gy and compare the survival rates, we find an average of 25 weeks' survival for those receiving a higher dose, and 26 weeks for those receiving a lower dose.

The pathological data from Asbury et al. on 14 patients irradiated at MITR indicates that all of the patients died from cerebral related causes. These included severe radiation necrosis of the brain, regrowth of tumors, massive intracranial hemorrhage, and acute bacterial meningitis. But even here, the amount of necrosis, regrowth of tumors, and vessel changes does not correlate well with the calculated doses. For example, no radiation

Table 3-4: Summary of pathological results and estimates of absorbed dose to the tumor, normal brain, and blood capillaries at 3 cm below the cut surface for 16 patients treated at MIT from 1960 to 1961[10]

Patient	Pathological Findings	Date of NCT	Tumor dose (RBE Gy)	Brain dose (RBE Gy)	Capil. dose (RBE Gy)
No. 1 (S.E.)	Tumor recurrence in area opposite to irradiation. Extensive radiation necrosis of brain and vessels.	Nov 15, 60	47.9	19.1	35.4
No. 3 (G.S.)	Massive intracranial hemorrhage. No residual tumor or necrosis found.	Nov 30, 60	31.9	12.7	23.6
No. 4 (P.D.)	Extensive tumor nodules on dura and surface of hemisphere.	Dec 30, 60	66.4	26.0	48.9
No. 5 (H.C.)	Extensive recurrence of tumor throughout the brain. Mild vascular damage.	Jan 6, 61	34.7	15.3	26.3
No. 6 (H.G.)	No residual tumor found. Extensive radiation necrosis and herniation of brain.	Jan 18, 61	42.0	15.6	30.6
No. 7 (J.D.)	No data available.	Jan 25, 61	86.6	30.4	62.3
No. 8 (F.L.)	Tumor recurrence in the fornix and adjacent medial thalamus. Extensive radiation necrosis of brain.	Jan 31, 61	115.4	40.6	83.0
No. 9 (S.W.)	Several nests of tumor near resected site. Damage of cervical cord and medulla related to radiation.	Feb 15, 61	57.7	20.3	41.5
No. 11 (N.L.)	Several islands of tumor. Extensive radiation necrosis of brain.	Mar 21, 61	150.6	52.4	108.1
No. 12 (C.F.)	No data available.	Apr 12, 61	75.3	26.2	54.1
No. 13 (N.J.)	Tumor recurrence found in area opposite to irradiated zone. Extensive radiation necrosis in irr. side.	Apr 18, 61	130.1	47.7	94.4
No. 14 (P.P.)	No data available.	May 3, 61 Jul 19, 61 Total	93.2 88.8 182.0	32.8 31.2 64.0	67.1 63.9 131.0
No. 15 (S.W.)	Tumor recurrence near resection area. Extensive radiation necrosis of brain.	May 16, 61	79.9	28.1	57.5
No. 16 (G.G.)	Extensive tumor infiltration and radiation necrosis.	Jun 30, 61	84.4	29.6	60.7
No. 18 (M.J.)	Tumor recurrence near resection area. Acute bacterial meningitis.	Aug 4, 61	124.3	43.7	89.4
No. 19 (M.H.)	No data available.	Aug 18, 61	104.3	36.7	75.0

damage was noted in patient No. 18 (M.J.), even though, he received one of the highest doses during the trial. On the other hand, patient No. 1 (S.E.), who received approximately 1/3 the dose that patient No. 18 received, was found to have severe radiation necrosis of the brain and vessels.

3.3.2 Second clinical series at MITR (1961-1962)

The next series of patients irradiated at MITR differed from the first series in two ways. First, they were injected with a new boron agent. This compound, sodium perhydrodecaborate ($Na_2B_{10}H_{10}$) was tested extensively by Soloway and Sweet and found to be superior to p-carboxyphenylboronic acid in several ways:[11] 1) this compound had a far greater percentage of boron per weight; 2) it was also less toxic then the previous compound (doses of 50 mg per kg of body weight could be given without deleterious effect); 3) it maintained its tumor-to-brain ratio far better than the p-carboxy-compound. Whereas in the previous compound, the T/B ratio fell to 4 after about an hour, the new compound maintained a ratio of 7:1 for over 3 hours in mouse gliomas.

The second improvement was that now the reactor could be operated at twice the power level. This reduced the irradiation time by half and thus afforded the physician the possibility to further optimize the time between the injection and the irradiation.

In the second series, two patients were treated with these new improvements. Table 3-5 summarizes the treatment conditions and the length of survival after NCT. For these patients, only the concentration of boron given was available. Although it is difficult to interpret trends from just two data points, the results are worse than in series one. Both patients showed no improvements following therapy and died soon thereafter.

Table 3-5: Summary of clinical trials at MIT (1961-1962)

Patient	Sex	Age	Date of Surgery	Date of NCT	Amount of ^{10}B Given	Neutron Fluence Given	Days Survival Post NCT
No. 20 (W.C.)	F	48	July 61	Aug 22, 61	30 ppm	2.50 E+13	11 wks
No. 21 (H.S.)	F	31	3 wks prior to irr.	N/A	30 ppm	~2.50 E+13	2 wks

Table 3-6 shows the summary of the pathological findings and my estimates for the absorbed dose to the tumor, the normal brain, and to the capillaries in a manner similar to table 3-2. There were two differences from the first series. The first difference is that the boron concentration factors have been changed to 2.92 and 0.47 for the tumor and brain respectively. This was based on clinical distribution studies made on human subjects by Sweet et al. and reflects the increased tumor to brain ratio obtained by the new compound. The second difference is the tumor to blood ratio have been changed to 0.79.[12]

Both patients died of severe cerebral edema and were worse after treatment than before. In the first patient, there was regrowth of tumors deep in the brain as well as radiation damage near the surface for normal brain.

Table 3-6: Summary of pathological results and estimates of absorbed dose to the tumor, normal brain, and blood capillaries at 3 cm below the cut surface for 2 patients treated at MIT from 1961 to 1962[12]

Patient	Pathological Findings	Date of NCT	Tumor dose (RBE Gy)	Brain dose (RBE Gy)	Capil. dose (RBE Gy)
No. 20 (W.C.)	Evidence of recurrent tumor in the deep tissue. Radiation damage to the scalp and the surface of the brain.	Aug 22, 61	82.9	27.4	38.8
No. 21 (H.S.)	Died of severe cerebral edema.	N/A	N/A	N/A	N/A

[Missing pages refer to clinical trials conducted in Japan]

REFERENCES

1. G. Locher, "Biological effects and therapeutic possibilities of neutrons," *American Journal of Roentgenology*, 1936, 36: 1-13.

2. D. Gabel, S. Foster, and R. Fairchild, "The Monte Carlo Simulation of the Biological Effect of the $^{10}B(n,\alpha)^{7}Li$ Reaction in Cells and Tissues and Its Implication for Boron Neutron Capture Therapy," *Radiation Research*, 1987, 111: 14-25.

3. H. Hatanaka, "Introduction," Boron-Neutron Capture Therapy for Tumors, Nishimura Co., Niigata, Japan, 1986.

4. W. Sweet, "The uses of nuc ear disintegration in the diagnosis and treatment of brain tumor," *New England Journal of Medicine*, 1951, 245: 875-878.

5. W. Sweet and M. Javid, "The possible use of neutron-capturing isotopes such as boron-10 in the treatment of neoplasms. 1. Intracranial Tumors," *Journal of Neurosurgery*, 1952, 9: 200-209.

6. L. Farr, W. Sweet, J. Robertson, C. Foster, H. Locksley, D. Sutherland, M. Mendelson, and E. Stickley, "Neutron capture therapy with boron in the treatment of glioblastoma multiforme," *American Journal of Roentgenology*, 1954, 71: 279-291.

7. J. Godwin, L. Farr, W. Sweet, and J. Robertson, "Pathological study of eight patients with glioblastoma multiforme treated by neutron capture therapy using boron 10," *Cancer*, 1955, 8: 601-615.

8. O. Deutsch and B. Murray, "Monte Carlo dosimetry calculation for boron neutron capture therapy in the treatment of brain tumors," *Nuclear Technology*, 1975, 26: 320-339.

9. L. Farr, J. Robertson, E. Stickley, H. Bagnall, O. Easterday, and W. Kahle, "Recent advances in neutron capture therapy," Progress in Nuclear Energy Series VII - Medical Sciences Vol. 2, London, Pergamon Press, 1959, 128-138.

10. A. Asbury, R. Ojemann, S. Nielsen, and W. Sweet, "Neuropathogic study of fourteen cases of malignant brain tumor treated by boron-10 slow neutron capture radiation," *Journal of Neuropathology and Experimental Neurology*, 1972, 31:278.

11. W. Sweet, A. Soloway, and G. Brownell, "Boron-slow neutron capture therapy of gliomas," *Acta Radiology*, 1963, 1: 114-121.

12. W. Sweet, "Final report on grant # AT(30-1) 1093 The use of thermal and epithermal neutrons in the treatment of neoplasms," from private notes.

13. H. Hatanaka, and K. Sano, "A revised boron-neutron capture therapy for malignant brain tumours, I. Experience on terminally ill patients after Co-60 radiotherapy,' *Journal of Neurology*, 1973, 204:309-332.

14. H. Hatanaka, "Eighteen autopsy cases of malignant brain tumors treated by boron-neutron capture therapy between 1968 and 1985," Boron-Neutron Capture Therapy for Tumors, Nishimura Co., Niigata, Japan, 1986.

15. H. Hatanaka, "A revised boron-neutron capture therapy for malignant brain tumors, II. Interim clinical result with the patients excluding previous treatments," *Journal of Neurology*, 1975, 209:81-94.

16. H. Hatanaka, "Clinical experience of boron-neutron capture therapy for gliomas - a comparison with conventional chemo-immuno-radiotherapy," Boron-neutron capture therapy for tumors, Nishimura Co., Niigita, Japan, 1986.

17. K. Jellinger, "Present limits of conventional treatment for malignant brain tumors," Boron-neutron capture therapy for tumors, Nishimura Co., Niigita, Japan, 1986.

18. W. Sweet, "Supplementary pharmacological study between 1972 and 1977 on purified mercaptoundecahydrododecaborate," Boron-neutron capture therapy for tumors, Nishimura Co., Niigita, Japan, 1986.

Herb Jacksley + Sweet Have

Sweet Soloway + Wright Have

Chapter Four

EPITHERMAL NEUTRON BEAMS FOR BORON NEUTRON CAPTURE THERAPY

4.1 INTRODUCTION

After the dismal failure in the United States of using thermal neutron beams for Boron Neutron Capture Therapy in the 50's and early 60's, no significant further attempts were made in the United States to treat brain tumors using NCT. As described in the preceding chapter, the failures were caused by three factors: 1) the lack of proper boron compounds that would permit high tumor to blood ratio of boron-10, 2) the poor understanding the physicians had of the importance of blood dose, and 3) the lack of neutron source that would permit treatment to depths greater than 3~4 cm in tissue.

The first factor was the poor tumor-seeking characteristics of the boron-loaded drugs that were administered to the patients before neutron irradiations. Although the tumor to normal brain ratio was high for these drugs (borax, sodium pentaborate, p-carboxybenzeneboronic acid, and sodium perhydrodecaborate), the tumor to blood ratio was often less than 1. This resulted in an enormous dose (sometimes > 100 Gy) being delivered to the walls of the

capillaries, causing swelling and failure of the vessels. During the pathological examinations, it was discovered that most brains had suffered from late ischemic injury (damage caused by starvation), which was caused by radiation-induced occlusion of the vascular supply. This in turn was caused by the damage to the endothelial cells of the capillary walls. In 1968, Hatanaka demonstrated this by duplicating similar damage in the brains of cats irradiated at MITR after administration of perhydrodecaborate, the same boronated agent used for clinical trials at MIT.[1]

The second related factor was the poor understanding the physicians had concerning the importance of the boron concentration in blood. It wasn't until the pathological reports were completed that they realized the cause of the deaths. Unfortunately, the first clinical trials at BNL suffered from exactly the opposite reason (not enough dose was given to cause damage) and could not be used to guide the clinical trials at MIT. Although the therapists understood the importance of a high tumor-to-brain concentration of boron, they could not predict that the blood capillaries would be the limiting organ in NCT. Therefore, their boron delivery schedule optimized on the highest tumor-to-brain ratio rather than the highest tumor-to-blood ratio.

The third reason was the innate characteristics of the thermal neutron beam itself. Figure 4-1 shows a typical thermal neutron flux vs. depth profile in a hydrogenous phantom for both the incident thermal neutron beam and the incident epithermal neutron beam. The thermal neutron beam peaks at the surface, whereas the epithermal beam peaks at about 2 cm into the phantom. Because the dose resulting from the boron capture reaction is directly proportional to the concentration of ^{10}B and the thermal neutron flux, those tissues containing boron near the surface, in the case of the thermal neutron beam, can receive a extremely high dose.

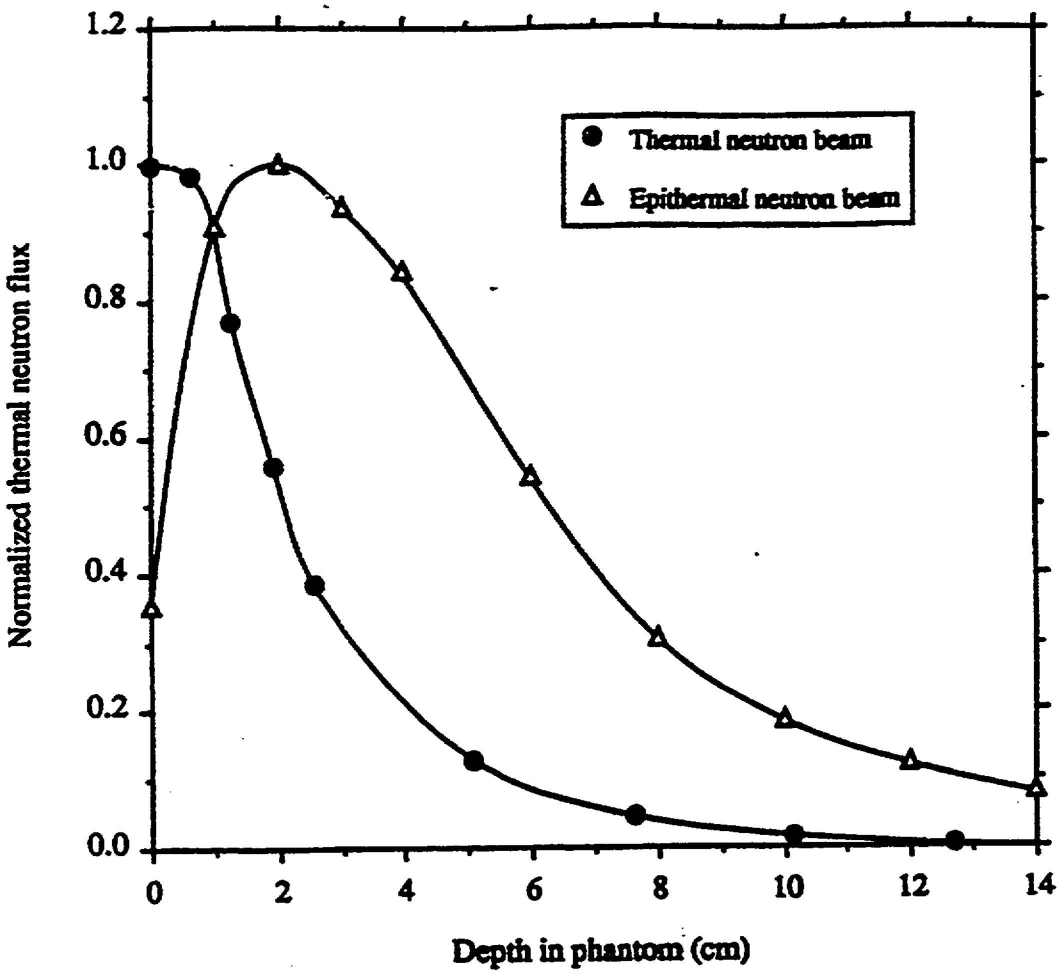


Figure 4-1: Thermal neutron flux profile from a typical thermal neutron beam and an epithermal neutron beam in a cylindrical hydrogenous phantom; normalized to their peak thermal neutron flux.

In the case of some early BNL and MIT/MGH clinical trial patients, they suffered from all three reasons. High concentration of boron in the blood combined with the high thermal neutron flux peak at the surface resulted in the highest dose being absorbed by the scalp for those patients treated at BNL. To reduce this effect, the later patients in the MIT/MGH trials and patients treated by Hatanaka in Japan had their scalps and skulls surgically reflected before therapy. However, such procedures have been shown to increase the chances of hemorrhage and infection and would not be practical in cases of fractionated neutron capture therapy. Two patients from the MIT trials and a number of others from Hatanaka's trials died as a direct result of complications resulting from surgical procedures conducted during neutron capture therapy.[2,3]

A means exists to eliminate the need for open craniotomies during irradiation and to increase useful thermal neutron flux at depth. This is to use an epithermal neutron beam for NCT. As shown in Figure 4-1, this epithermal beam has a peak to surface thermal neutron flux ratio of over 3. This means that through the use of epithermal neutron beams, the boron induced radiation dose in the capillaries near the surface of the brain can also be reduced by a significant margin, minimizing the chances for incurring serious radiation damage to the scalp. In addition, the penetrability of the neutrons is significantly increased. The epithermal neutron beam shown has a higher thermal neutron flux at 6 cm than it does at the surface.

One way to assess neutron beam qualities is to use the three figures of merit introduced at the BNCT workshop held at MIT in March of 1989.[4] These are the advantage depth (AD), the advantage ratio (AR), and the advantage depth dose rate (ADDR). These concepts are illustrated in figure 4-2. Advantage depth is that depth at which the total dose received by the tumor, containing some predetermined concentration of boron, equals the highest total background dose received by healthy tissue anywhere in the radiation field. Distinction is made between the maximum advantage depth (AD_{max}) and the minimum advantage depth

NEUROPATHOLOGIC STUDY OF FOURTEEN CASES OF MALIGNANT BRAIN TUMOR TREATED BY BORON-10 SLOW NEUTRON CAPTURE RADIATION*

ARTHUR K. ASBURY, M.D.†,
ROBERT G. OJEMANN, M.D.,
SURL L. NIELSEN, M.D.‡,
AND
WILLIAM H. SWEET, M.D., D.Sc.
(Boston, Mass.)

INTRODUCTION

Between 1951 and 1961 a systematic attempt to utilize the special advantage of boron 10-slow neutron capture radiation to treat primary malignant brain tumors was made at the Massachusetts General Hospital and at Brookhaven National Laboratories (1–6). Clinical experience at these two institutions has been reported previously (7-9). No patients have been radiated for brain tumor by this technique since 1961 because the method as utilized offered no advantage over standard methods of therapy already available.

The present communication is a neuropathologic study of fourteen brains from the series of patients at the Massachusetts General Hospital who were irradiated at the Massachusetts Institute of Technology nuclear reactor between 1959 and 1961. In addition to standard neuropathologic study of these brains, a topographic analysis of tissue change was carried out in relation to local neutron flux. It is uncertain how closely neutron flux corresponds to actual local tissue dosage of radiation because the exact boron-10 levels at each site are not known. With this qualification in mind, neutron flux is taken as a first approximation of radiation dose.

Historical Background

Theoretical and experimental work on the possible utilization of boron-slow neutron capture therapy in the treatment of brain tumors has been summarized in a number of previous reports (1–5, 7–10). While the possibility of treating neoplasms by the technique of neutron capture radiation was realized as early as 1936, it was not until 1951 that the use of a boron-neutron interaction was suggested for the treatment of brain tumors (11).

The rationale for this type of therapy rests upon the fact that two distinct moieties, boron-10 and thermal neutrons, each innocuous by itself in the doses used, interact to pro-

---

From the Charles S. Kubik Laboratory of Neuropathology of the James Homer Wright Laboratory of Pathology, and the Neurosurgery Service, Massachusetts General Hospital, Boston, Mass. 02114.

Supported in part by U.S.P.H.S. Training Grant NS 05393 and A.E.C. contract AT (30-1)-1093.

* Presented in part at the 40th annual meeting of the American Association of Neuropathologists, Atlantic City, New Jersey, June 13–14, 1964.

† ‡ Present Address: Departments of Neurology† and Pathology‡, University of California at San Francisco, Parnassus Avenue, San Francisco, California 94122.

Exhibit 1
22981

L001921

:ASES OF
·ORON-10
N*

pecial advantage
malignant brain
l at Brookhaven
institutions has
. for brain tumor
ffered no advan-

fourteen brains
spital who were
lear reactor be-
: study of these
it in relation to
sponds to actual
·els at each site
taken as a first

·ron-slow neutron
: in a number of
by the technique
1951 that the use
iors (11).
distinct moieties,
, interact to pro-

:s Homer Wright
General Hospital.

.C. contract AT

:ation of Neuro-

:ity of California

…ce a high energy nuclear reaction with the resulting fragments sharing between them 2.4 …llion electron volts (Mev):

$$^{10}_{5}B + ^{1}_{0}n \rightarrow [^{11}_{5}B] \rightarrow ^{7}_{3}Li + ^{4}_{2}He + 2.4 \text{ Mev}$$

The mass and the charges of the particles evolved in this fission (despite their enormous energy) preclude their travel for more than a short distance, therefore, the radiation injury is confined to that distance, a radius of roughly ten microns from the site of the capture reaction (Fig. 1). The requirement of two components, boron-10 and thermal neutrons, to produce this destructive radiation and the short range of the emitted particles are attractive features possessed by no other current form of radiation therapy. Neutron capture offers the potential advantage of delivering a much higher radiation dose selectively to tumor cells if they contain large concentrations of boron-10.

The utilization of boron compounds in the treatment of cancer has revolved about the unique nuclear property of the nonradioactive boron-10 isotope to absorb thermal neutrons. The two boron isotopes, ^{10}B and ^{11}B, differ greatly in this property. Whereas ^{11}B, with a normal abundance of 80.4 per cent, has a capture cross section for thermal neutrons of 0.05 barns, boron-10, with an abundance of 19.6 per cent, has a capture cross section of 3850 barns. It

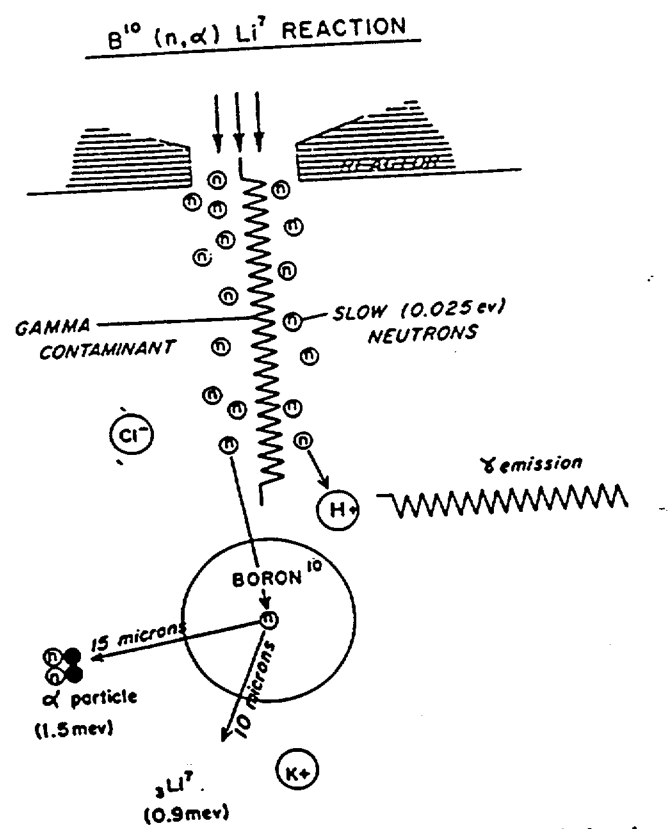


FIG. 1. Schematic diagram of nuclear and radiational events during boron 10-slow neutron capture radiation.

MIT 1001922

TABLE I

Clinical Data

Case no.	Age	Sex	Tumor type	Location	Onset to 1st op. (mos.)	1st Op. to neut. Rx (mos.)	Course prior to neut. Rx	Boron dose mg/kg	Route	Neutron flux at brain surface (× 10¹²/cm²)	Radiation time in minutes	Course after neutron Rx	Neutron Rx to death (mos.)	Onset to death (dur. of illness, mos.)	Other rad.
1	14	M	Astrocytoma low grade	Right cerebellar hemisphere	115	10	2 prior resections, still functioning	20	IV	1.0	15	Obtunded, febrile, CSF fistula	115	13	2000 r/port × 3 ports
2	81	F	Glioblastoma	Right frontal lobe	6	12	Did well for first year, then rapid decline	15	IV	1.1	75	Rapidly declining course continued	2	20	None
3	20	F	Amelanotic melanoma	Right temporal lobe	6	3	Headache & diplopia the major problems	21	IV	2.0	90	Headache mainly until final months, then rapid decline	1	12	L-phenylalanine mustard 1 mo. prior to death
4	35	M	Glioblastoma	Left temporal lobe	6	2	Mainly incr. pressure symptoms, even after 2 craniotomies	25	IV	1.1	15	Sank into stupor after 4 weeks & remained so	4	13	1000 r
5	61	M	Glioblastoma	Left frontal lobe	5	1	Rapidly progressive hemiparesis from outset	24	IV	3.3	105	Continued decline	4	10	None
6	40	F	Glioblastoma	Right parietal lobe	2	1	Progressive hemiplegia & mental defect	31	IV	3.3	165	Sank into coma & remained so	5	8	None
7	11	M	Medulloblastoma	Posterior fossa	4	1	Increased pressure, papilledema & ataxia	30	IV	1.3	90	Normal for 1 mo. Then progressive cervical myelopathy	7	12	2000 r in final mo. of life
8	30	F	Glioblastoma	Left parietal lobe	1	315	Headache, seizures & inc. aphasia	20	IV	1.5	45	Relatively intact for 10 mos. Then rapid decline	1135	18	None
9	48	F	Glioblastoma	Left frontal lobe	1	31	Rapidly progressive impairment	30*	IC	2.5	60	Comatose in 2 weeks & remained so	215	4	None
10	59	F	Glioblastoma	Left temporo-parietal lobe	27	2	Rare seizures & mild aphasia with slow acceleration in course	30	IV	2.0	75	Slow decline continued until final weeks	6	35	None
11	21	M	Glioblastoma	Left frontal lobe	81	20	Occasional seizures for 7 years, then accelerating course with operations	30	IV	1.9	60	Accelerating course with seizures, aphasia and stupor	4	108	5000 r and L-phenylalanine mustard
12	67	M	Glioblastoma	Right parieto-occipital lobe	12	1	Gradually accelerating non-dominant parietal syndrome	30	IV	1.8	60	Immediate course unchanged (rest unknown)	7	20	None
13	24	F	Glioblastoma	Left parietal lobe	15	35	Weak right arm with focal seizures only	30*	IC	2.0	30	Comatose with increased pressure	15	[illegible]	None
14	46	M	Glioblastoma	Left temporal lobe	1	15	Rapidly progressive aphasia and torpor	30	IV	2.0	60	Unimproved. Died of bacterial meningitis	2	316	None

TABLE I

Clinical Data

Case no.	Age	Sex	Tumor type	Location	Onset to 1st op. (mos.)	1st Op. to neut. Rx (mos.)	Course prior to neut. Rx	Boron dose† mg/kg	Route	Neutron flux at brain surface (X 10¹²/cm²)	Radiation time in minutes	Course after neutron Rx	Neutron Rx to death (mos.)	Onset to death (dur. of illness, mos.)	Other rad.
1	16	M	Astrocytoma low grade	Right cerebellar hemisphere	11½	10	2 prior resections, still functioning	20	IV	1.0	45	Obtunded, febrile, CSF fistula	1½	13	2000 r/port X 3 ports
2	51	F	Glioblastoma	Right frontal lobe	6	12	Did well for first year, then rapid decline	15	IV	1.4	75	Rapidly declining course continued	2	20	None
3	20	F	Amelanotic melanoma	Right temporal lobe	5	3	Headache & diplopia the major problems	21	IV	2.0	90	Headache mainly until final months, then rapid decline	4	12	L-phenylalaninemustard 1 mo. prior to death
4	35	M	Glioblastoma	Left temporal lobe	6	3	Mainly incr. pressure symptoms, even after 2 craniotomies	25	IV	1.1	45	Sank into stupor after 4 weeks & remained so	4	13	1000 r
5	41	M	Glioblastoma	Left frontal lobe	5	1	Rapidly progressive hemiparesis from outset	26	IV	3.3	105	Continued decline	4	10	None
6	48	F	Glioblastoma	Right parietal lobe	2	1	Progressive hemiplegia & mental defect	31	IV	3.3	105	Sank into coma & remained so	5	8	None
7	14	M	Medulloblastoma	Posterior fossa	4	1	Increased pressure, papilledema & ataxia	30	IV	1.3	90	Normal for 4 mos. Then progressive cervical myelopathy	7	12	3600 r in final mo. of life
8	30	F	Glioblastoma	Left parietal lobe	1	3½	Headache, seizures & inc. aphasia	20	IV	1.5	45	Relatively intact for 10 mos. Then rapid decline	11½	18	None
9	48	F	Glioblastoma	Left frontal lobe	1	¾	Rapidly progressive impairment	30*	IC	2.5	60	Comatose in 2 weeks & remained so	2½	4	None
10	59	F	Glioblastoma	Left temporo-parietal lobe	27	2	Rare seizure & mild aphasia with slow acceleration in course	30	IV	2.6	75	Slow decline continued until final weeks	6	35	None
11	34	M	Glioblastoma†	Left frontal lobe	81	20	Occasional seizure for 7 years, then accelerating course with operations	30	IV	1.9	60	Accelerating course with seizures, aphasia and stupor	4	104	5000 r and L-phenylalanine mustard
12	57	M	Glioblastoma	Right parieto-occipital lobe	12	1	Gradually accelerating non-dominant parietal syndrome	30	IV	1.8	60	Immediate course unchanged (rest unknown)	7	20	None
13	24	F	Glioblastoma	Left parietal lobe	½	½	Weak right arm with focal seizures only	30*	IC	2.0	30	Comatose with increased pressure	1½	1½	None
14	48	M	Glioblastoma	Left temporal lobe	1	1½	Rapidly progressive aphasia and torpor	30	IV	2.9	60	Unimproved. Died of bacterial meningitis	2	3½	None

* [illegible]

was on the basis of this unusual property that the use of boron-10 and other nuclides with high capture cross section was proposed as a means of selectively destroying brain tumors. Capture cross section refers to the apparent area presented by an atom for thermal neutrons and is expressed in barns, whereby 1 barn is defined as being equal to 1×10^{-24} cm^2.

The feasibility of this procedure is also based upon the fact that normal elements of tissue have low capture cross-section values for thermal neutrons H = 0.32. C = 0.0045. O = 0.001. N = 1.7. Na = 0.45. K = 2.05 and Cl = 32.5 barns (5). While the cross section values are small by comparison with boron-10, these atoms are present in such large concentration that their absorption of neutrons does contribute to the total radiation dose. The two major sources of such radiation are from the hydrogen and nitrogen atoms:

$$^1_1H + ^1_0n \rightarrow (^2_1H) \rightarrow ^2_1H + \gamma$$

$$^{14}_7N + ^1_0n \rightarrow (^{15}_7N) \rightarrow ^1_1P + ^{14}_6C$$

However, with a boron-10 concentration in the tumor of 50 mg kg of tissue and a neutron flux of 1.25×10^9 neutrons/cm^2/sec, 86 per cent of the total radiation dose would result from the boron-10 capture reaction. Thus, the destructive radiation would predominate in those areas having high boron-10 concentrations (8). Thermal neutrons themselves are sub-ionizing since they carry a charge of 0.024 electron volts. No appreciable effect from direct thermal neutron radiation has been reported (3).

In 1954 Farr, Sweet and co-workers (2) reported the results of treatment in a series of patients with glioblastoma multiforme at the nuclear reactor at the Brookhaven National Laboratory. After intravenous administration of a boron-10 compound, irradiation of the tumor was carried out through intact scalp. Ten patients received a total of 21 treatments. Both by clinical and pathological criteria (6) the radiation had a negligible effect on tumor and brain, with the exception of the first patient in whom massive necrosis of the temporal lobe tumor might have been partially a radiation effect. It did suggest to us the advisability of considering suction removal of tissue debris some weeks after treatment. However, radiation had a devastating effect on the overlying scalp. The reason for this differential effect between scalp and deeper-lying tumor was the high neutron flux in the superficial tissue, combined with a high concentration of boron.

Review of Clinical Aspects of the Present Series

A total of 18 patients received 19 irradiations. Table I summarizes the clinical and radiational details. The preradiation diagnosis in all patients with a supratentorial tumor was glioblastoma multiforme, although one of these was subsequently shown to be an amelanotic melanoma. Two posterior fossa tumors were treated, one a medulloblastoma and the other an astrocytoma, Grade II. In all cases a craniotomy was performed sometime prior to the irradiation to establish the diagnosis and to resect as much gross tumor mass as possible. An interval of at least 3 weeks was then allowed for the blood-brain barrier in the surrounding normal tissue to reconstitute (12). Each patient was then taken to the operating room beneath the MIT reactor and the craniotomy wound reopened with reflection of scalp, bone, and dura. The surrounding scalp was protected with boron-free plastic and small bags containing lithium fluoride; an air-filled balloon was placed in the operative cavity to keep normal brain from collapsing into the wound. Continuous suction kept the cavity dry. Fine gold wires (5–6 cm. in length) and small gold foils were then placed on the surface of the dura and brain and within its substance, and the position of each was recorded. After these preliminary preparations a lithium fluoride collimator was attached over the operative area. Following radiation the gold wires and foils were removed and the neutron flux in the area was determined from the neutron activation of the gold.

Sixteen patients were given an intravenous injection of paracarboxybenzene boronic acid containing boron-10 and two patients received sodium perhydrodecaborate via intracarotid injection. These two compounds were selected after testing of numerous boron compounds for their ability to localize in mouse glioma tumors, their toxicity, and, finally, their selec-

tive uptake by malignant human brain tumors. Previous reports have summarized these investigations (8, 13, 14).

METHODS

Brains were fixed by immersion in 10% formalin, although in several instances specimens were received from other institutions already fixed. When the brains were sectioned, an attempt was made to cut them in the same planes in which the fine gold wires had been placed during neutron exposure. Large blocks, usually hemispheral in size, were embedded in celloidin, cut at 12 to 18 microns, and stained with hematoxylin and eosin, cresyl violet, and Loyez method for myelin. Where indicated, smaller tissue blocks were made for frozen sections, and stained for astrocytes by the Cajal gold sublimate method, for axons by the Cajal silver technique, for sudanophilic lipids using Scharlach R, and for glial fibrils by the Holzer method. Selected celloidin sections were stained with phosphotungstic acid-hematoxylin, with the silver method of Foot for reticulin, with the Verhoeff-van Giesen stain for elastic tissue, with periodic acid-Schiff reagent for aldehyde groups, and with Congo red for amyloid.

Topographic analysis of neutron flux was carried out in the following manner. Neutron flux in different areas and at specific tissue depths was calculated after measurement of the activation of the gold wires and foils. Points of known neutron flux were plotted directly on hemispheral microscopic sections which were intentionally cut in the planes in which the gold wires and foils had been placed at craniotomy (see Review of Clinical Aspects for details). Allowance was made arbitrarily for 15% shrinkage of tissue during preparation.

As control material, four cases of glioblastoma multiforme, either untreated or treated by partial surgical excision only, were comparably processed and surveyed. In addition, one of us (AKA) examined the pathologic material from twenty cases of intracranial neoplasm treated by boron-10 neutron capture through the intact scalp; these cases were reported in 1962 by Farr et al (9). An extensive series of "control" glioma specimens prepared at the Warren Anatomical Museum was surveyed at the same time.

RESULTS

Clinical Features

Pertinent facts concerning the course of each patient are listed in Table I. Eleven of the fourteen patients had a malignant glioma (glioblastoma multiforme) by all criteria. Each had had one or more previous craniotomies, at which the tissue diagnosis was established. In case three, whose tumor type is listed as an amelanotic melanoma, the clinical diagnosis was believed to be malignant glioma until late in the course of the illness when the true nature of the tumor became evident. The primary source was never determined. Single cases of medulloblastoma (case 7) and of grade II astrocytoma (case 1), both posterior fossa neoplasms, were also radiated.

All of the patients were dead within a year after neutron capture treatment, and eleven of the fourteen were dead after six months. The clinical course was generally well-advanced when this therapy was undertaken. In every instance, the cause of death at post mortem examination was cerebral in nature, specifically extensive radiation necrosis of brain in nine (cases 4-10, 12 & 13), and a combination of extensive tumor infiltration and radiation necrosis in one (case 11), recurrent tumor in two (cases 2 & 3), massive intracranial hemorrhage in one (case 1), and acute bacterial meningitis in one (case 14).

Histopathological Observations

In the interest of simplicity, pathological description has been divided into four groups according to the major brain lesions observed, which in all cases was the presumptive cause of death. A summary of the neuropathological

orts have summarized the

i several instances specimens
e brains were sectioned, as
he fine gold wires had been
eral in size, were embedded
-lin and eosin, cresyl violet
blocks were made for frozen
e method, for axons by the
R, and for glial fibrils by
with phosphotungstic acid.
h the Verhoeff-van Gieson
aldehyde groups, and with

following manner. Neutron
d after measurement of the
i flux were plotted directly
cut in the planes in which
iew of Clinical Aspects for
issue during preparation.
either untreated or treated
surveyed. In addition, one
s of intracranial neoplasm
iese cases were reported in
specimens prepared at the

in Table I. Eleven of the
me) by all criteria. Each
gnosis was established. In
the clinical diagnosis was
ness when the true nature
termined. Single ... s of
1), both posterior fossa

ire treatment, and eleven
s generally well-advanced
of death at post mortem
necrosis of brain in nine
nfiltration and radiation
ssive intracranial hemor-
).

has been divided into
d, which in all cases
he neuropathological

findings in each case may be found in Table II. In the illustrations (Figs. 2–11, 13), a major emphasis has been placed upon the histopathological nature of the radiation necrosis encountered in group I. Figs. 12, 14–17 depict the extent and distribution of residual neoplasm and radiation necrosis in cases in group I.

I. Radiation necrosis (cases 4-13). In the gross state, every brain showed evidence of swelling, either generally or limited to one cerebral hemisphere, with flattening of gyri and compression against the free edges of the dura mater. Some of the specimens showed significant distortion of the midbrain. Where most of the tumor, and hence the beam of radiation, was localized to one cerebral hemisphere, it was the more swollen, usually with subfalcine herniation of the cingulate gyrus and transtentorial herniation of the medial temporal lobe (Fig. 2). Evidence of previous surgical excision of cerebral tissue was obvious, often with gelatinous coagulum filling the residual cavity. Zones of radiation damage were usually well demarcated, and were characterized by coagulation necrosis with no tendency towards liquefaction. In the more acutely evolving cases (cases 9, 13), brain swelling was more prominent, and the necrotic areas had a pink coloration due to diffuse extravasation of red blood cells. The consistency of acutely necrotic areas was slightly softer than normal with a grainy friability and a tendency to crumble when cut. In those instances in which survival following radiation was 4 months or more, areas of necrosis were yellow-gray in color, and sometimes were less well demarcated. The general shape and outline of necrotic tissue was retained, but tissue markings of cortex and white matter tracts and nuclei were lost and replaced by a mottled grainy appearance. These zones were less friable than normal and had a tougher, leathery consistency with no evidence of liquefaction.

On microscopic examination, a stereotyped pattern of pathological changes was observed (Fig. 3–10). Broad fields of coagulation necrosis were noted with disappearance of all recognizable parenchymal elements save for the skeletons of thickened blood vessels and the gnarled remains of astrocytic processes (Fig. 4). Myelin stains showed broad zones of pallor, sometimes homogeneously pale (Fig. 11), but more often with a mottled pallor with rings of clearing around blood vessels producing both a punctate and coalescent pattern (Fig. 3, 13A). Generously sprinkled throughout were the hematoxyphilic fragments of innumerable cell nuclei, primarily polymorphonuclear leucocytes (Fig. 4). Only minor phagocytic activity was noted, and almost no sudanophilia was detectable in frozen sections exposed to fat stains (Fig. 7). Near the edges of necrotic zones, heavy astrocytic gliosis was apparent on Holzer and Cajal gold stains (Fig. 10), and frequent swollen distorted astrocytic processes were present throughout the areas of necrosis.

Changes in the blood vessels were distinctive, and are worthy of special comment. At the earliest time following radiation at which radiation effect could be seen (case 13, Fig. 5), an acute necrotizing lesion of vessels of all sizes was prominent. The vessel walls were smudged by fibrin impregnation, and a brisk polymorphonuclear response was evident. Endothelial nuclei were plump and swollen, and frequently thrombosed vessels were found. In later stages (case

TABLE II

Summary of Neuropathological Observations

Case no.	Final diagnosis	Features of previous biopsies	Residual tumor extent and character	Radiation necrosis extent and character	Other processes
1	Astrocytoma	Grade II astrocytoma	None discovered	None discovered	Massive midbrain hemorrhage. Meningitis over left cerebellar hemisphere.
2	Glioblastoma	Large zones gemistocytic in character	Extensive infiltration of entire left hemisphere, corpus callosum, and remaining right frontal lobe	Mild vascular thickening and perivascular lymphocytic infiltration in right frontal lobe	
3	Amelanotic melanoma	Melanoma in cervical node	Extensive tumor nodules on dura and surface of hemispheres; tumor encased brainstem and spinal cord	Non-specific vessel changes, mostly in residual temporal lobe	Scattered small infarcts
4	Glioblastoma	Extreme anaplasia and necrosis	None discovered	Massive necrosis with swelling; herniation of left hemisphere	
5	Glioblastoma	Necrosis and palisading	Islands of tumor posterior to op. site, and in opposite frontal lobe	Extensive necrosis of exposed medial surface of right frontal lobe; also for 5 cm. posterior to left frontal resection margin	
6	Glioblastoma	Necrosis and palisading	Several islands of tumor	Extensive necrosis up to 6 cm. from op. bed involving both hemispheres. Severe swelling	
7	Medulloblastoma	No atypical features	A half-dozen nests of tumor cells near resection margins, over medulla, and in adjacent meninges	Swelling and softening of upper cervical cord and lower medulla, presumably related to radiation. Gray columns most severely affected	Pyramidal tract degeneration lower in spinal cord

				[illegible] from op. bed involving both hemispheres. Severe swelling	
7	Medulloblastoma	No atypical features	A half-dozen nests of tumor cells near resection margins, over medulla, and in adjacent meninges	Swelling and softening of upper cervical cord and lower medulla, presumably related to radiation. Gray columns most severely affected	Pyramidal tract degeneration lower in spinal cord
8	Glioblastoma	Typical with giant cells	Definite tumor nests in left hemisphere, [illegible] directly in op. site	Widespread necrosis of left hemisphere spreading into corpus callosum. Extreme vessel changes	Calcification of necrotic debris deep in lesion
9	Glioblastoma	Severe anaplasia and pleomorphism	Mod. extensive tumor infiltration in inferior portions of both frontal lobes	Severely swollen, widespread necrosis of anterosuperior left frontal lobe. Discrete demarcation	Ant. cerebral arteries occluded by rad. lesion
10	Glioblastoma	Cellular but not undifferentiated	Infiltration of fornix and adjacent medial thalamus	Necrosis of much of inferior left hemisphere extending to thalamus, also in upper pontine tegmentum and left cerebellar hemisphere	Secondary degeneration of pyramidal tract in brainstem
11	Glioblastoma	All grades of glioma	Extensive infiltrate in left hemisphere and right frontal lobe	Severe necrosis in frontal lobes, left greater than right. Up to 5 cm. extent from op. cavity	
12	Glioblastoma	No atypical features	Tumor with giant cells in medial occipital lobe near resection margin	Severe necrosis of posterior right hemisphere extending 7–8 cm. anterior from occip. pole. Also necrosis in midbrain	
13	Glioblastoma	No atypical features	Subpial tumor layer adjacent to resection margin extending into op. site	Massive swelling and necrosis of left hemisphere with widespread necrotizing lesion of vessels	Necrosis not coagulative as in other cases
14	Glioblastoma	None available	Glioma cells in left temporal resection margin	None discovered	Acute purulent meningitis. Cocci in leucocytes

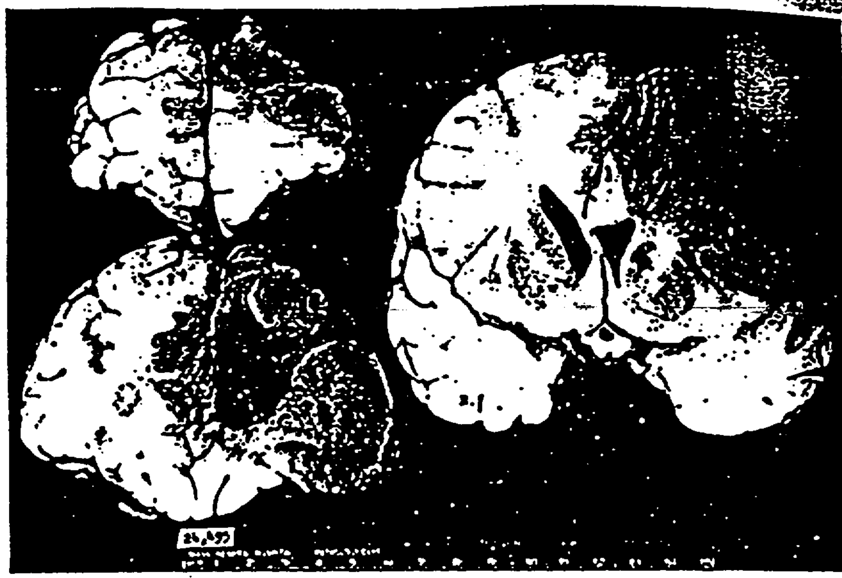


FIG. 2. Coronal sections of brain (case 9) showing extensive radiation necrosis of left frontal lobe with swelling. The cavity filled with gelatinous material in the slice at lower left represents the operative defect.

6, Fig. 6), the inflammatory reaction and fibrin exudation were even more prominent, and an adventitial proliferative response began to thicken the vessel walls. Plump, swollen endothelial and perithelial nuclei persisted. As the process evolved, medial and adventitial proliferation of connective tissue continued to thicken vessel walls, and the acute inflammatory response was replaced by a more indolent, primarily lymphocytic, infiltrate (Figs. 7, 8). In the patient surviving the longest (case 8. Fig. 9), blood vessels showed extreme degrees of thickening and fibrosis of their walls. PAS stains were strongly positive in such vessel walls, but no congophilia was present. Veins as well as arteries were involved, and all sizes of vessels from capillaries to major named arteries were affected if they lay within the field of radiation necrosis.

Some residual tumor infiltrate was demonstrable in every instance in this group except one (case 4), and its relationship to zones of radiation necrosis is shown in the topographic diagrams (Fig. 12, 14–17). Fairly extensive tumor was present in two specimens (cases 9, 12), and definite islands of glioma cells were found in the others (cases 5–8, 10, 13). These were at times directly in the path of the radiation beam and close to previous resection margins.

Radiation necrosis was generally more visible in white matter than gray, and was more intense at the brain surface where the highest neutron flux was measured. In some instances, however, the process extended deep within the brain and to distant structures (Fig. 11, 13A).

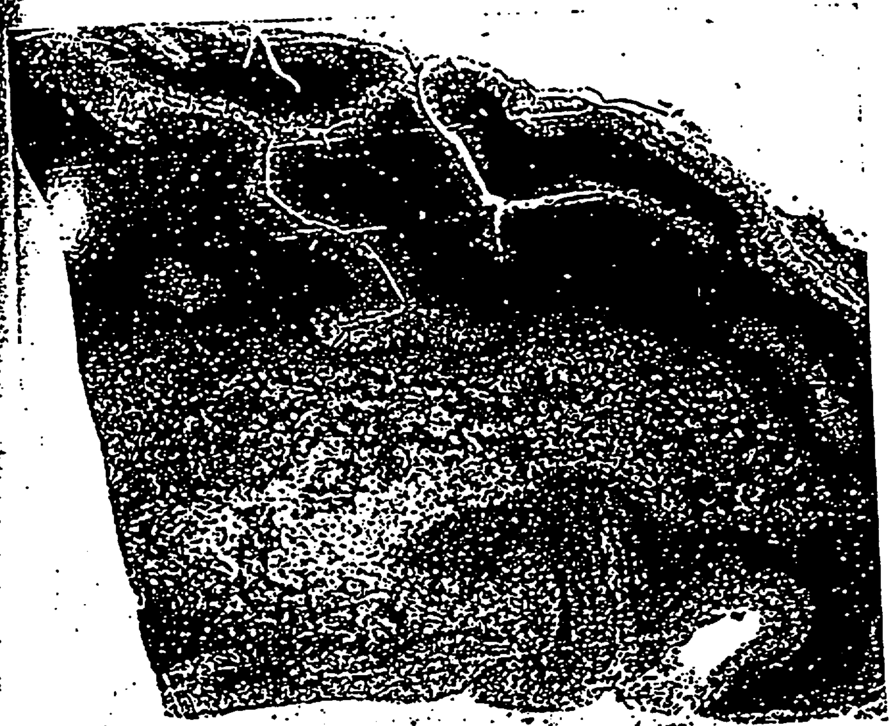
radiation necrosis of left
rial in the slice at lower

tion were even more
n to thicken the vessel
rsisted. As the process
ve tissue continued to
se was replaced by a
7, 8). In the patient
ed extreme degrees of
ongly positive in such
well as arteries were
named arteries were

very instance in this
radiation necrosis is
irly extensive tumor
slands of glioma cells
times directly in the
margins.
matter than gray, and
st neutron flux was
ded deep within the

In case 11, it was not possible to decide which of two processes was preeminent, radiation necrosis or residual tumor (see Fig. 17). The features of radiation necrosis observed were identical to those described in the preceding section. All grades of glioma were present, from well-differentiated, low-grade astrocytoma to anaplastic pleomorphic zones typical of glioblastoma multiforme. From the long clinical course and the histological appearance of the neoplasm as seen in the biopsy taken at craniotomy and in the autopsy specimen, it is likely that this patient had a low-grade astrocytoma which underwent progressive malignant degeneration.

Special mention should be made of case 7, in which the posterior fossa was radiated for medulloblastoma. Severe softening of the upper cervical cord and lower medulla was striking, but did not exhibit the degree of coagulation necrosis of parenchyma or the extent of vessel changes which were so prominent in the cerebral hemispheres of other cases (Fig. 13B). The anterior spinal artery showed significant endothelial swelling and fibrosis of its wall, although the



F. 3. Low power view of a horizontal section of the right parieto-occipital lobe (case 12) showing extensive radiation necrosis, primarily of white matter. Note the mottled character of the lesion with more pronounced zones of myelin pallor surrounding blood vessels. (Loyez stain; 2.5×)

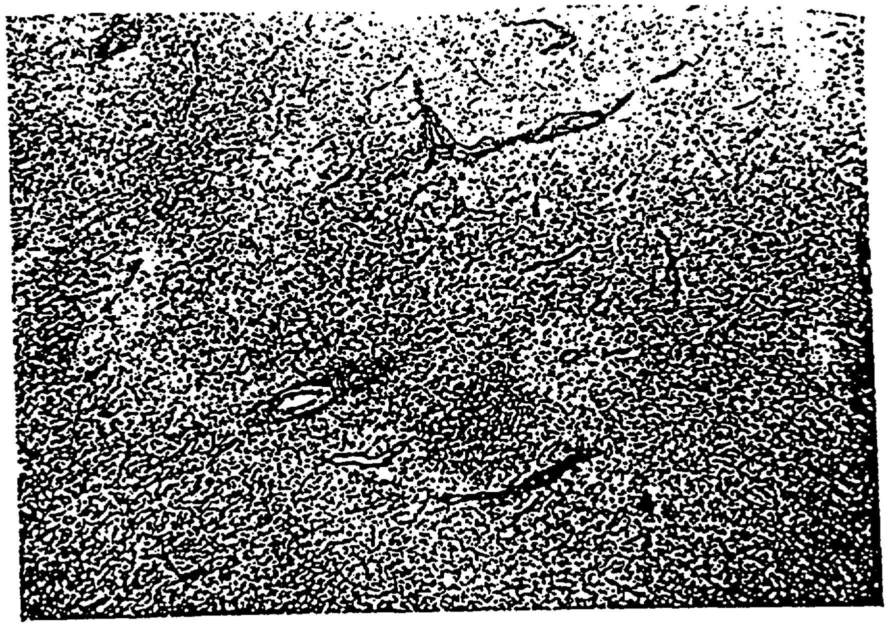


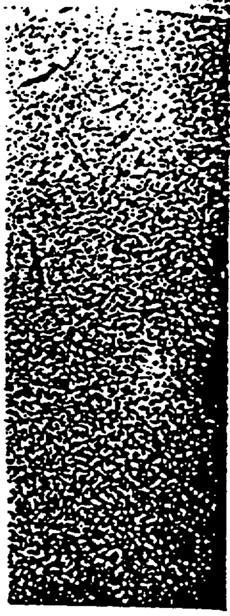
FIG. 4. Low power view of coagulation necrosis due to radiation. All tissue elements are devitalized, and large amounts of undigested cellular debris are present. Hematoxylin and eosin stain; 30×; case 9).

vessel was not found to be occluded at any of the levels examined. Nevertheless, the pattern of the lesion did suggest that ischemia played an important role.

Comment: The prominence and extent of radiation change in this group was the most striking feature of the whole series. The pathological material spans a post-radiation interval of 10 days to 11½ months, and gives a clear indication of the temporal evolution of the lesion from acute radiation necrosis (case 13) to typical delayed radiation necrosis (case 8), particularly in terms of blood vessel changes.

II. Residual tumor (cases 2, 3). In two cases, the predominant finding was residual tumor; nests of tumor were found in most of the cases in the other groups, but were not considered to be the major pathological process.

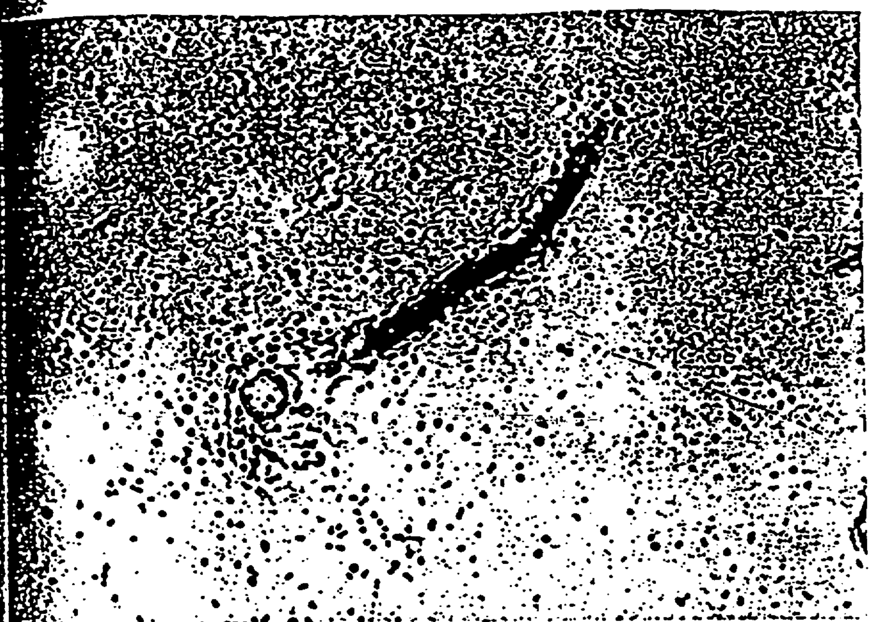
In case 2, the right frontal lobe was absent to a coronal level approximately 2 cm. posterior to the temporal tip, and the resection margin was yellow-brown and smooth. The brain was not swollen grossly, and there was little evidence of tumor infiltration upon naked eye inspection; however, by microscopic examination there was extensive infiltration of typical glioblastoma multiforme in the remaining right frontal lobe, the corpus callosum, and the entire left frontal lobe with a thick shell of tumor partially encircling the left lateral ventricle extending posteriorly as far as the left occipital lobe. Moderate thickening of blood vessel walls with some perivascular infiltration of lymphocytes was pres-



All tissue elements are ... sent. Hematoxylin and

mined. Nevertheless,
n important role.
ge in this group was
cal material spans a
es a clear indication
n necrosis (case 13)
y in terms of blood

ominent finding was
e cases in the other
process.
vel approximately 2
n was yellow-brown
as little evidence of
microscopic exami-
a multiforme in the
entire left frontal
ft lateral ventricle
erate thickening of
phocytes was pres-



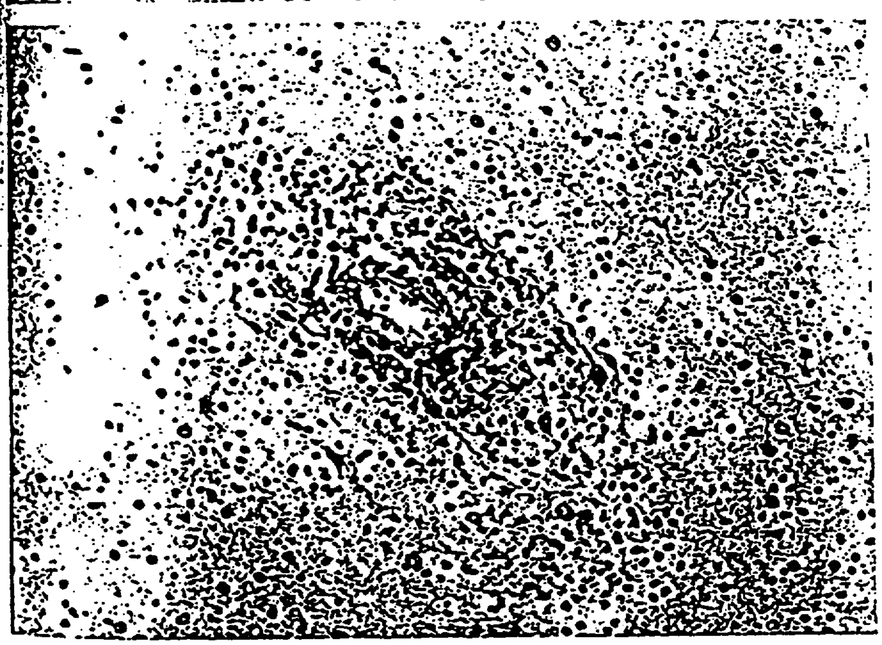


FIG. 5. Acute blood vessel necrosis and thrombosis with prominent endothelial nuclear swelling and polymorphonuclear leucocytic response 10 days after radiation (Hematoxylin and eosin stain; 100×; case 13).

FIG. 6. Acute vascular and perivascular reaction 5 months after radiation. The vessel wall is beginning to thicken, and fibrin exudation as well as a polymorphonuclear leucocytic response is seen in the surrounding tissue. (Hematoxylin and eosin stain; 110×; case 6).

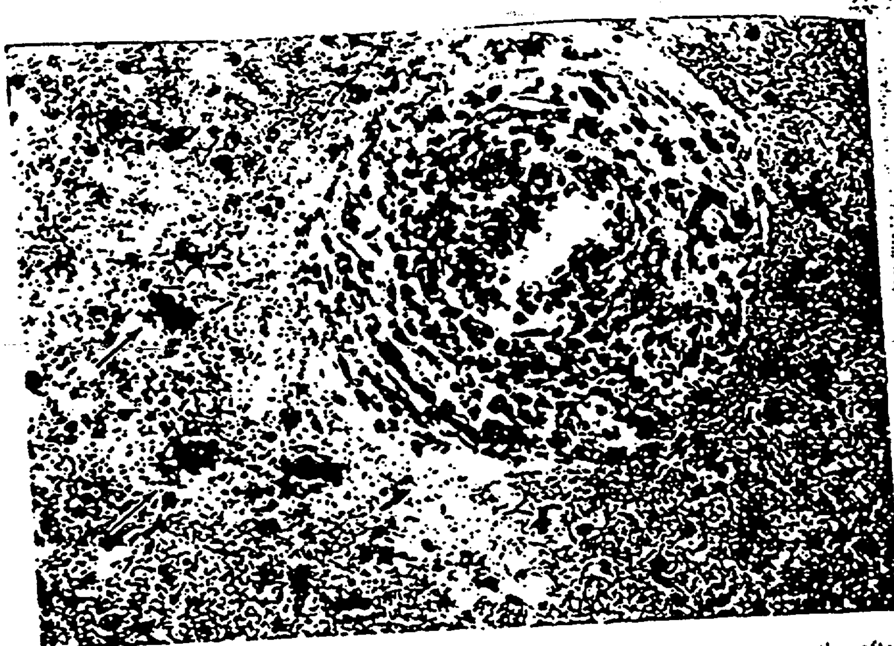


FIG. 7. Extensive proliferation and infiltration in blood vessel wall 5 months after radiation in an almost completely necrotic field. Some sudanophilic material is seen in cells at left (arrows). (Scharlach R stain; 250×; case 6).

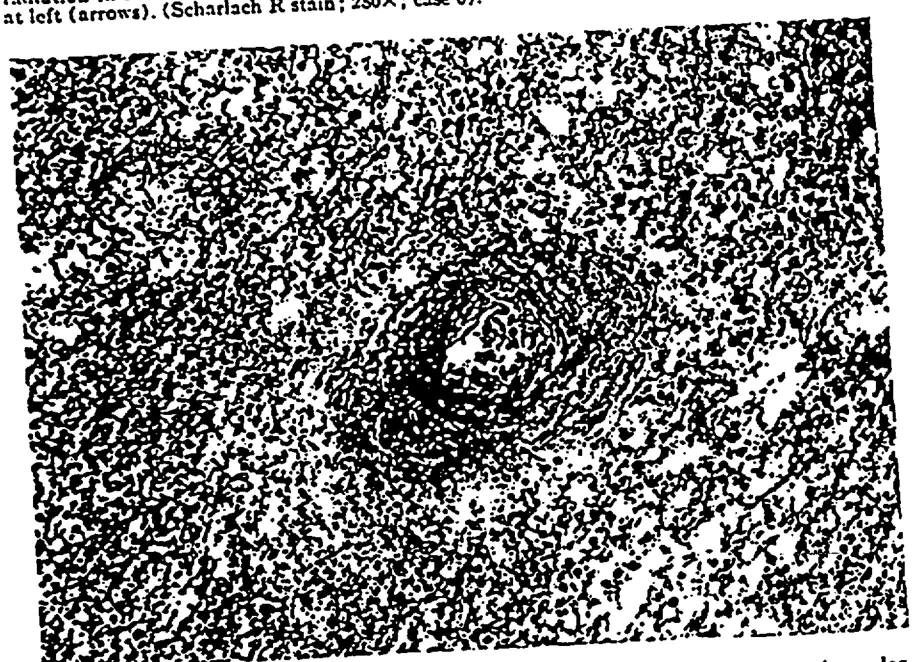


FIG. 8. Blood vessel thickening 11½ months after radiation with minimal perivascular lymphocytic infiltrate. (Phosphotungstic acid hematoxylin stain; 150×; case 8).

.1 5 months after
rial is seen in cells

F. . 9. Extreme degree of vascular reaction 11½ months following radiation. (Hematoxylin eosin stain; 220×; case 8).

FIG. 10. Fibrillary astrocytosis which was prominent in incomplete lesions and at the edges of zones of complete tissue destruction. (Cajal gold chloride sublimate stain; 400×).

nimal perivascular
ase 8).

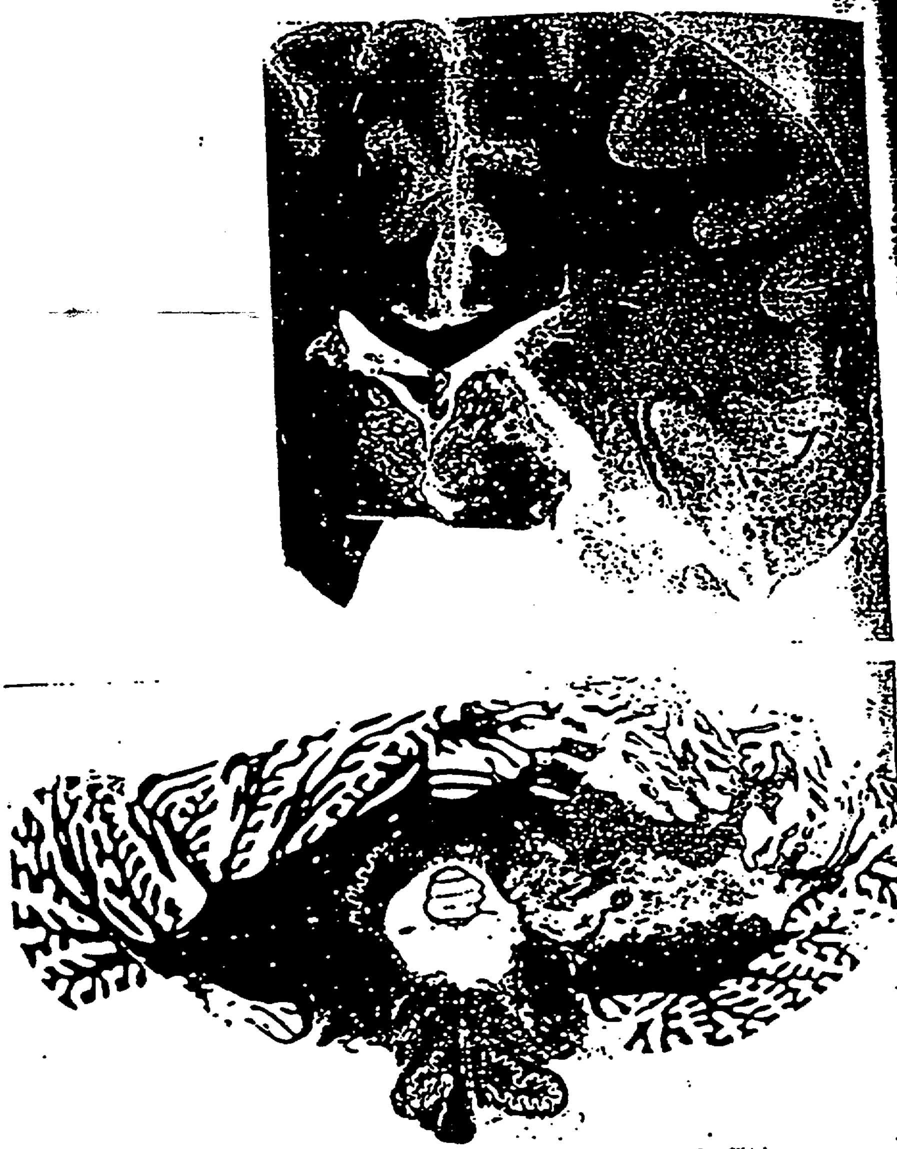


Fig. 11. Large sections of cerebral hemispheres (upper) and brain-stem and cerebellum (lower) stained for myelin showing the extent of myelin pallor. Note the relatively sharp border of demarcation in the lateral thalamus and in the cerebellum. Tract degeneration in the left pyramid is evident. The hemispheral section (upper) corresponds to the diagram in Fig. 12A. (Loyez stain; upper 1.0×; lower 1.4×; case 10).

n and cerebellum
e relatively sharp
t degeneration in
to the diagram in

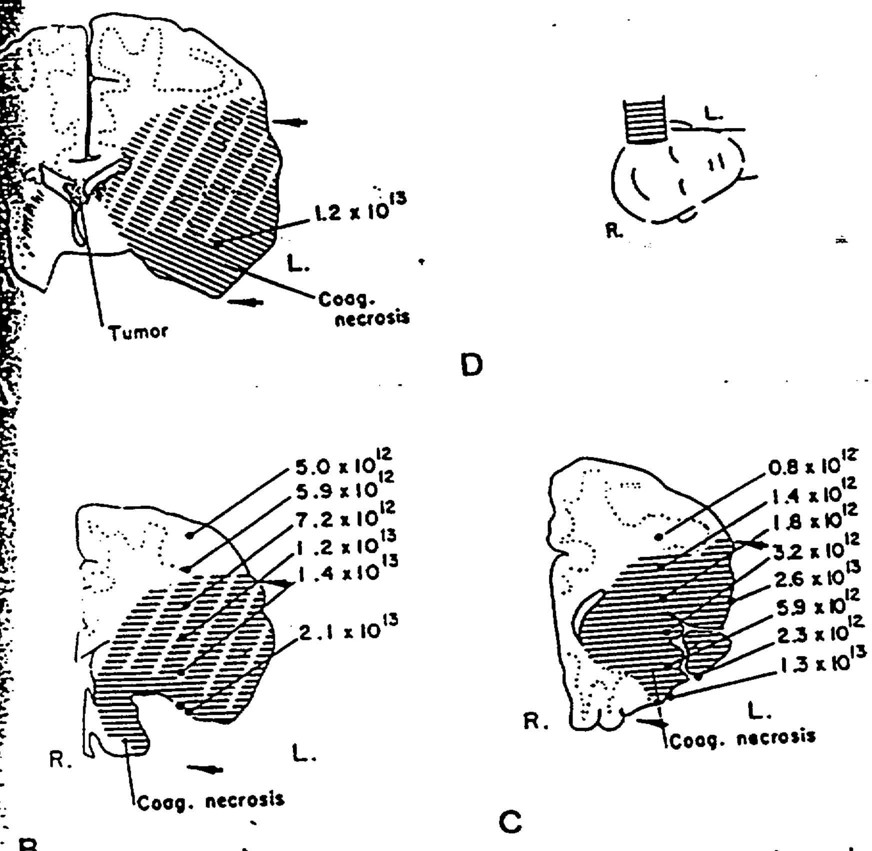


Fig. .. Line diagrams of sections from case 10 with neutron flux determinations as indicated. Tissue boron levels are uncertain. (A) temporo-parietal lobe; (B&C) left frontal lobe; (D) attitude of neutron collimator with respect to the head. Arrows at brain surface represent the edge of the collimator. Hatched areas are radiation necrosis, and semi-hatched areas represent incomplete radiation damage. Stippled areas in fornix and left thalamus (A) are residual tumor.

ent near the right frontal resection margin, but this change could not be ascribed to radiation with any certainty.

In case 3, innumerable lobulated nodules of gray-white fleshy tumor were adherent to the inner surface of the dura mater bilaterally; these indented and occasionally penetrated the underlying cortical surface, in places to a depth of a centimeter or more. The base of the brain was encased in a 3–4 mm. layer of tumor tissue which engulfed the optic nerves and chiasm, the pituitary stalk, and the olfactory lobes, and extended posteriorly over the surface of the pons and medulla. The walls of the third ventricle were studded with tumor nodules. Tumor sheets up to 4 mm. in thickness enveloped almost the entire spinal cord

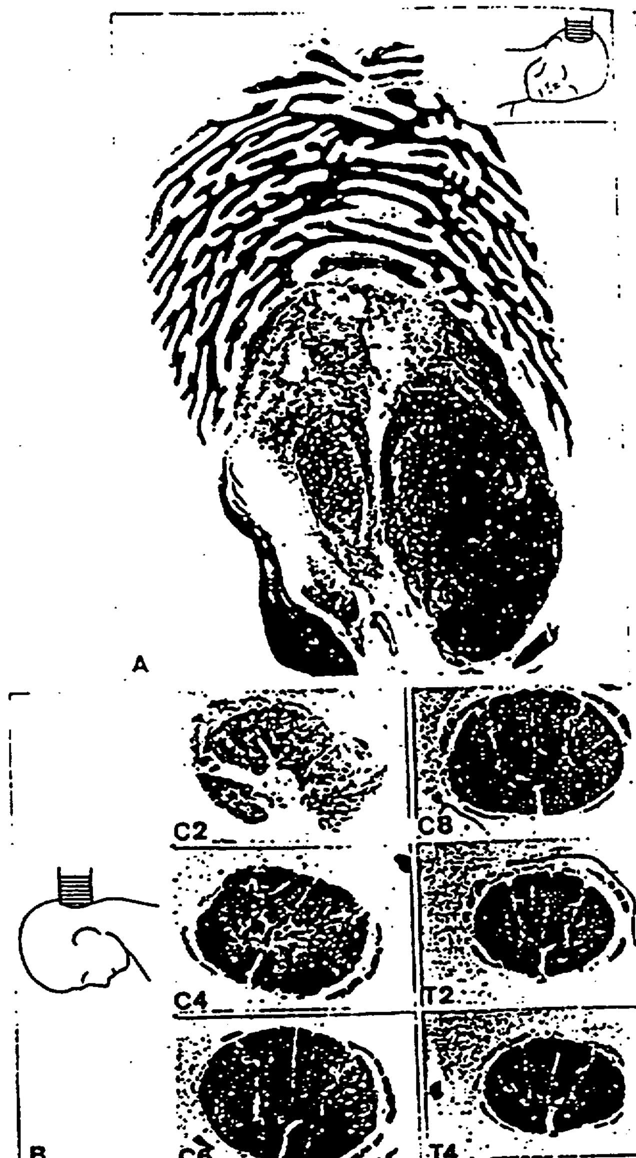


FIG. 13. (A) Midbrain and superior pole of cerebellum stained for myelin showing mottled coagulation necrosis due to radiation in the tectum. This is at some distance from the origin of the neutron beam (see insert). The cerebral peduncle at left has been distorted by compression. (Loyez stain; 3.5×; case 6). (B) Extensive softening of upper cervical cord 7 months following posterior fossa radiation. The insert at left indicates the positioning of the neutron beam collimator. See Table II and Results section, Group I for details. (Heindenhain stain for myelin; 2.5×; case 7).

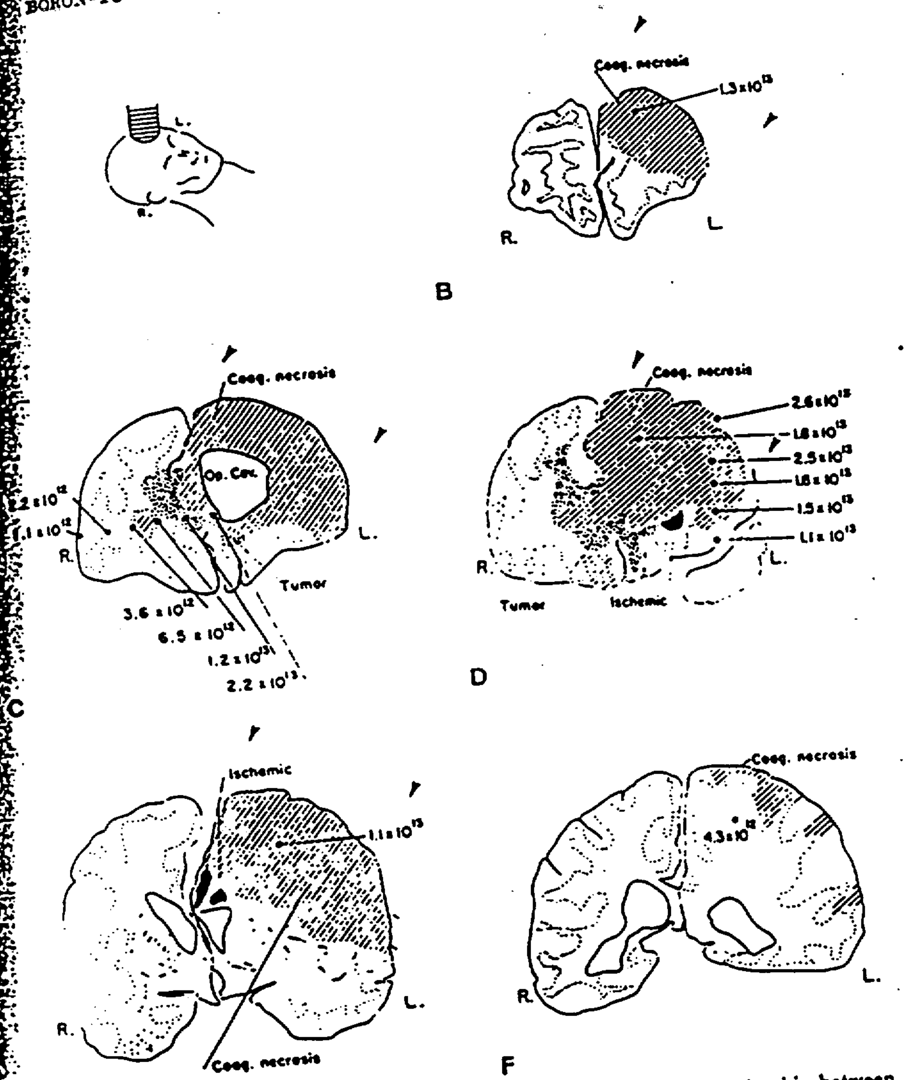


FIG. 14. Line diagrams of five coronal sections from case 9 showing relationship between radiation necrosis, residual tumor, and neutron flux. (A) Position of collimator; (B, C, D, E, F) anterior to posterior hemispheral sections. The arrows at the brain surface indicate the edge of the collimator.

and most of the spinal roots as far as the cauda equina. Two small areas of lacunar infarction were identified in the right posterior thalamus. Microscopically the tumor was composed of large round or polygonal sharply outlined cells with marked pleomorphism and hyperchromatophilia. Mitotic figures, often

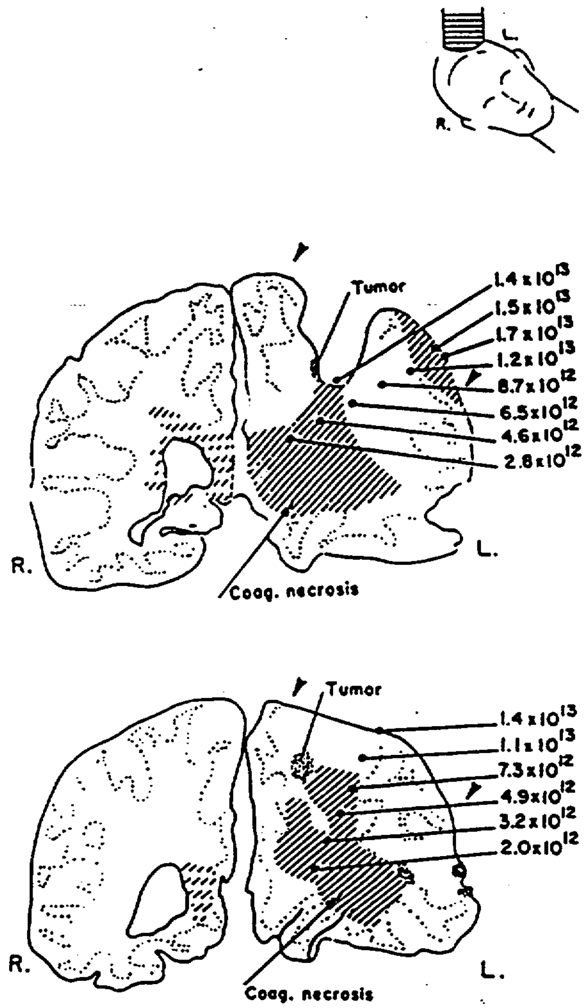


FIG. 15. Line diagrams of two coronal sections from case 8 showing relationship between radiation necrosis, residual tumor, and neutron flux. The position of the collimator is indicated at top. Semi-hatched areas represent incomplete necrosis, and the arrows at brain surface mark the edges of the collimator. The upper section is through the operative site and the lower section is approximately 1.5 cm. posterior.

bizarre, and multinucleated tumor giant cells were frequently seen. Examination of the other body organs showed metastatic tumor in liver, spleen, lung, ovary, spine, bone marrow, and bronchial lymph nodes. No definite changes could be attributed to radiation effect.

Comment: The first patient (case 2) was approaching the final stages of her illness when radiated, and died two months later of the primary brain tumor

0^{13}
$.0^{13}$
10^{13}
10^{13}
10^{12}
$.10^{12}$
$.10^{12}$
$x10^{12}$

10^{13}
10^{13}
10^{12}
$x10^{12}$
$.10^{12}$
$x10^{12}$

elationship between
: collimator is indi-
arrows at brain sur-
: operative site and

; seen. Examina-
ver, spleen, lung,
definite changes

inal stages of her
nary brain tumor

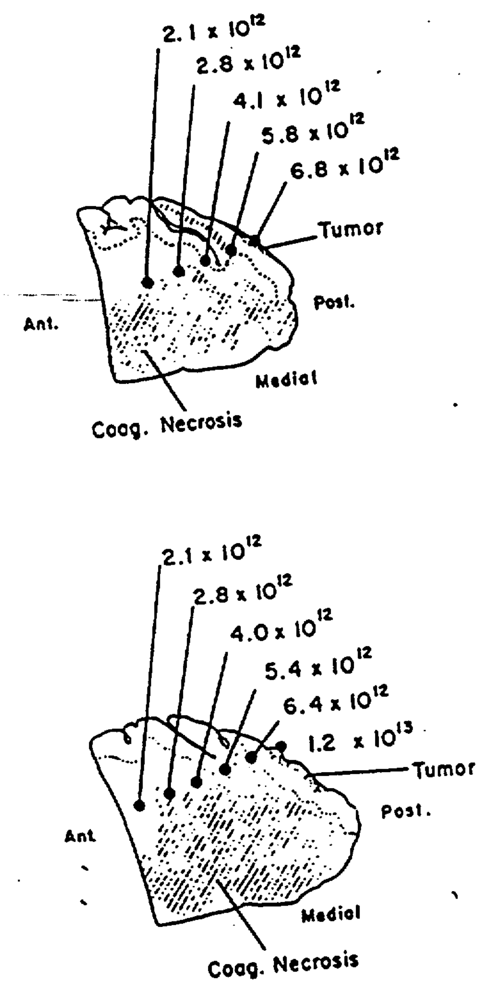


FIG. 16. Line diagrams of two horizontal sections of right parieto-occipital lobe from case 12 showing relationship between radiation necrosis, residual tumor, and neutron flux.

without alteration of the clinical decline. In the second patient in this group (case 3), extensive seeding of amelanotic melanoma over the surface of the entire neuraxis resulted in death, and no signs of radiation effect could be identified with confidence.

III. Intracranial hemorrhage (*case 1*). The cerebral hemispheres were severely swollen and compressed against the dura with flattening of convolutions. Below the tentorium, a massive hematoma filled the right side of the posterior cranial fossa with almost total destruction of the midbrain and right thalamus, and severe distortion and softening of the remaining brain stem and left cere-

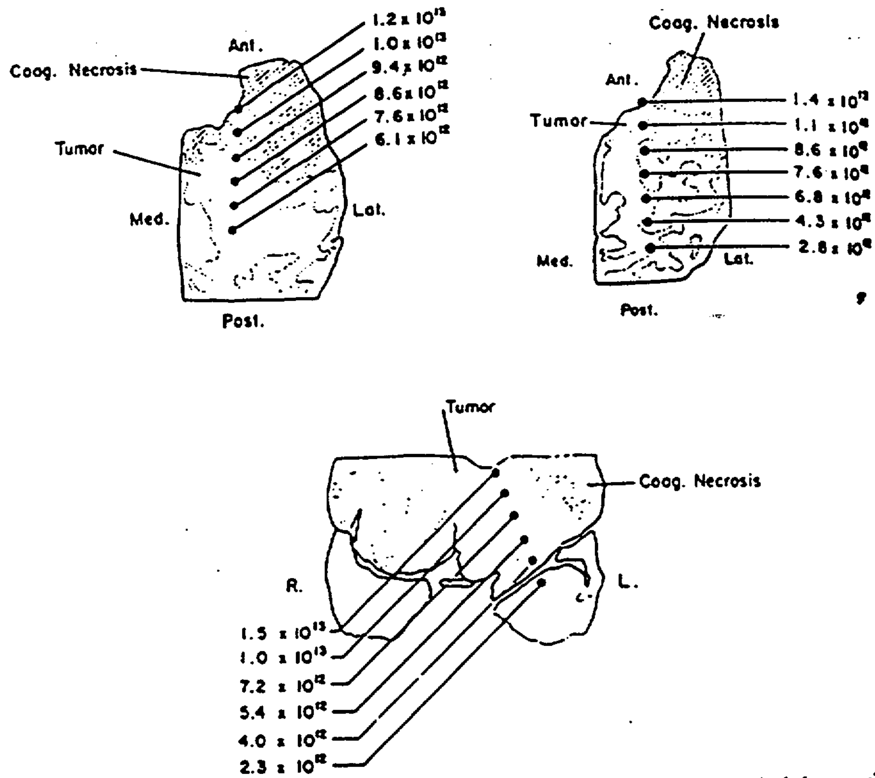
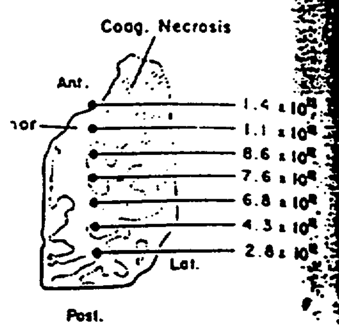
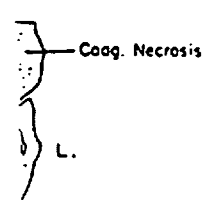


FIG. 17. Line diagrams from case 11 of two horizontal sections through left superior fronto-parietal lobe and a single coronal section at the level of the optic chiasm showing the relationship between radiation necrosis, extensive residual tumor, and neutron flux.

bellar hemisphere. Fresh blood had dissected into the left cerebellar hemisphere, pontine tegmentum, left thalamus and occipital lobe, and right lenticular nucleus; a cast of blood filled the lateral ventricles. Microscopic examination of pons, medulla, cerebellum, and remaining diencephalon disclosed normal vessels with no evidence of the type of radiation changes in blood vessel walls which were prominent in group I. Resolving purulent meningitis was observed between the folia and over the surface of the remaining left cerebellar hemisphere.

Comment: This patient did poorly following radiation with poor wound healing and a persistent cerebrospinal fluid fistula. One week prior to death a staphylococcal meningitis was diagnosed, and appeared to be under control when death due to massive hemorrhage supervened. Although the violence of the midbrain hemorrhage destroyed critical portions of the pathological specimen, the parts that remained and were examinable revealed no explanation for the hemorrhage. The characteristic blood vessel changes observed in many of the other longer surviving cases were not found here. This brain was one of two in which no residual tumor was detected.





l sections through left superior
vel of the optic chiasm showing
l tumor, and neutron flux.

.e left cerebellar hemisphere, be, and right lenticular nu- Microscopic examination of .lon disclosed normal vessels in blood vessel walls which ngitis was observed between erebellar hemisphere.

:adiation with poor wound One week prior to death a peared to be under control i. Although the violence of s of the pathological speci- revealed no explanation for anges observed in many of . This brain was one of two

Acute bacterial meningitis (case 14). An extensive surgical defect of the ior half of the left temporal lobe began 2.5 cm. behind the temporal tip and nded 8 cm. posteriorly. A thick, purulent exudate coated the surfaces of h cerebral hemispheres and the basal structures. Microscopically, an acute ymorphonuclear exudate was present in the subarachnoid spaces; a necrotiz- inflammatory lesion of many of the pial vessels was observed. Innumerable ci were present in the cytoplasm of leucocytes, primarily within the ventric- ar cavities and near the choroid plexus. Small zones of glioma were found in e left inferior temporal resection margin. No definite radiation changes were tectable.

Comment: This patient died of an intercurrent meningitis two months after diation. It is presumed that the atrium of the infection was related to the revious craniotomies.

DISCUSSION

The neuropathologic features of fourteen cases of malignant brain tumor reated by radiation at open craniotomy using boron 10-slow neutron capture ere surveyed. From the clinical standpoint, no therapeutic advantage was gained by this technique, because all of the patients were dead within a year. The average survival from the time of diagnosis (not the time of neutron capture radiation) was nine months, which was roughly the same average survi l for a similar large series treated by partial surgical resection and conv tional radiation, as reported by Taveras, Thompson, and Pool (15).

Pathologically, the outstanding feature in ten of the fourteen brains, and putative cause of death in nine, was radiation necrosis. The process was marked by coagulation necrosis of all parenchymal elements and striking blood vessel changes which became more prominent with the passage of time following radiation. From a qualitative standpoint, the changes due to radiation in these brains are distinctive, and would not be mistaken for the liquefactive events which characterize infarct necrosis. In a cerebral infarct, a predictable series of autolytic, reactive, and reparative events takes place, which includes softening of devitalized tissue, autolysis of tissue debris, migration of phagocytic cells intc e area of necrosis, and neovascularization. These events seemed to be suspended in the radiation necrosis demonstrated in this material, with the result that the tissue retained its shape, if not its architecture, and softening did not proceed to any extent. Fragments of destroyed cells, both parenchymal and reactive, remained undigested, giving the characteristic appearance of broad fields of finely granular chromatin debris and bits of astrocytic processes. Phagocytic activity and sudanophilia were almost absent, and proliferation and migration of microglia appeared to be suppressed. Neovascularization did not occur, but fibrin impregnation of damaged vessels was striking. Changes evolv- ing with the passage of time included gradual subsidence of the chronic perivas- cular inflammatory exudate and progressive thickening of blood vessel walls, ultimately to an extreme degree. Ablation of the reactive and reparative proc- esses ordinarily encountered in most crude cerebral lesions probably accounts

for the easily recognizable picture of large coagulated devitalized areas with undigested fragments of cellular debris.

This severity of necrotizing change has not often been described in [illegible] following radiation (16), but has been seen following attempts to excise [illegible] surgically a series of inoperable intracerebral tumors using the Bragg peak [illegible] of the proton beam (17). The acute radiation necrosis found in case 13 [illegible] days), and perhaps in case 9 (2½ months), resemble most closely the effects produced experimentally by gamma radiation in primates (18, 19). The remainder of the material showing radiation effect probably fits best in the category of delayed radiation necrosis (20). In any event, there is no evidence to suggest that the quality of pathological change we observed is peculiar to neutron capture radiation, but rather is a function of the intensity of radiation, regardless of its source.

Blood vessel changes were striking at all stages of the evolution of the radiation lesion. Although damage to the vascular network may be prominent secondary to radiation from any source, the pattern observed in our material at least raises the suspicion that boron may have sequestered in vessel walls, resulting in selectively high doses of radiation to those structures. This possibility must remain speculative until more is learned about boron distribution in tissues. We do know that there were higher levels of ^{10}B in the circulating blood than in the tumor at the time of radiation. In those patients given paracarboxybenzene boronic acid, the tumor: blood ratio in determinations during the first operation for gross removal of tumor averaged 0.50; in those given sodium perhydrodecarborate the average of 101 determinations was 0.79. Hence there were enough ^{10}B atoms in the blood stream near the endothelial linings to give a dangerous dose of radiation to these sensitive cells. It was the unequivocal realization of the need for a carrier for the ^{10}B which is largely cleared from the blood stream by the time of neutron radiation which led to cessation of the therapeutic trials.

In the present series, the extent of radiation damage and interval of delay following radiation correlated only in an approximate way with systemic boron-10 doses and neutron flux, and normal brain elements appeared to be as radiosensitive as neoplastic cells. A reasonably accurate measurement of neutron flux was possible, but obtaining an estimate of boron levels was less satisfactory. Blood and urine boron levels were determined before and after irradiation in many of the patients, and the concentration of boron in tumor and adjacent brain was obtained in a few instances immediately before and after irradiation. Although much is known experimentally of the relative boron levels of many tissues following injection of boron-10 (8, 13, 14, 21), the actual distribution within any given tissue is less well known. The isotope is thought to distribute equally in body water, but radiographic investigations aimed at deciding this point were inconclusive (22, 23).

Terao (24) has studied autoradiographically the distribution of the $B_{12}H_{11}SH$ and of $B_{12}H_{11}S\ SH_{11}B_{12}$ using a tritium label, stably incorporated into the boron hydride cage structure. In his animal model, the transplantable mouse

alized areas strewn
escribed in humans
pts to excise radio-
e Bragg peak effect
and in case 13 (10
closely the effects
8, 19). The remain-
t in the category of
evidence to suggest
peculiar to neutron
f radiation, regard-

e evolution of the
may be prominent
d in our material at
ed in vessel walls,
tures. This possibil-
oron distribution in
he circulating blood
given paracarboxy-
ons during the first
those given sodium
s 0.79. Hence there
lial linings to give a
as the unequivocal
is largely cleared
ich led to cessation

d interval of delay
way with systemic
s appeared to be as
easurement of neu-
ron levels was less
d before and after
of boron in tumor
ediately before and
f the relative boron
, 14, 21), the actual
e isotope is thought
stigations aimed at

on of the $B_{12}H_{11}SH$
corporated into the
ansplantable mouse

...dymoblastoma, the neoplastic cells grow in solid clusters with large loosely ...ure... extracellular spaces between. It was disconcerting to find the labelled ...pounds strikingly confined to the latter spaces so that many of the neoplastic ... would escape the capture radiation. In studies with transplantable rat ...blastomas developed by Benda et al (25), Amano (26), has used alpha-...oradiography to trace the disposition of $Na_2B_2H_{11}SH$. In highly preliminary ...ults it looks tentatively as though this compound in these tumors concen-...tes within the neoplastic cell proper. This is the more encouraging since the ...tologic appearance of these tumors is similar to that of the human glio-...stoma.

In the human case material, only rough estimates of average boron-10 con-...trations in tumor and adjacent brain could be made, and variation from site ... site within these tissues was completely unknown. The irregular character of ...diation lesions led us to suspect that boron levels varied greatly.

Another aspect concerns the ability of thermal neutrons to penetrate tissue. ...weet and Javid (4) have calculated the diffusion length of thermal neutrons, the distance at which the beam will be reduced to 1/e (½·178) of its original intensity, as 2.3 cm. for brain containing 12 mg./g of ^{10}B. Roughly then the neutron flux halved with each 2-cm. increment of depth within the brain, resulting in a reduction of surface neutron flux by almost an order of magnitude at a tissue depth of 6 or 7 cm. As pointed out previously, the relationship of local ... utron flux to radiation change was variable, both from case to case and within ... given case.

Residual tumor was discovered in all but two cases, and perhaps failure to find tumor in two represents a failure to carry out extensive enough sampling for microscopic examination. In those cases in which residual tumor was identified, it often occurred just distant to the furthermost zone of radiation necrosis (see Figs. 12, 14, and 17). In others, residual tumor was found in or near the operative site (see Figs. 15 and 16), an area that had presumably received heavy radiation. There are several possible explanations for such disparate observations. Tumor cells might have reinfiltrated the operative sites in the months since operation, or certain glioma cells may be so radioresistant that even ... presumptive high doses encountered in the tumor bed could not eradicate them. A third possibility concerns unequal cellular distribution of boron-10, so that some cells even in the tumor bed might escape radiation. Recent work of Amano (26) involving autoradiographic studies in rat glioblastomas revealed relatively homogeneous uptake of $B_{12}H_{11}SH$ throughout the viable cells, tending to exclude the discouraging third possibility.

SUMMARY

Neuropathologic observations on fourteen cases of malignant brain tumor treated by boron 10-slow neutron capture radiation at open craniotomy are prese... d. Extensive radiation necrosis was the major finding in nine, residual tumor ... two, a combination of radiation necrosis and tumor in one, massive intracerebral hemorrhage in one, and acute bacterial meningitis in one. Varying

amounts of residual neoplasm were detected in all instances except two, in which none could be found. Radiation necrosis was characterized by coagulation of devitalized tissue with failure of the usual liquefactive chain of events and by striking blood vessel affection. The relationship between radiation necrosis, residual tumor, and neutron flux is demonstrated topographically in several cases.

Acknowledgment: The guidance and advice of Dr. E. P. Richardson, Jr. are gratefully acknowledged.

REFERENCES

1. Brownell, G. L., and Sweet, W. H.: Studies on neutron capture therapy. Progr. Nucl. Ener., 2: 114–127, 1959.
2. Farr, L. E., Sweet, W. H., Robertson, J. S., Foster, C. G., Locksley, H. B., Sutherland, D. L., Mendelsohn, M. L., and Stickley, E. E.: Neutron capture therapy with boron in the treatment of glioblastoma multiforme. Amer. J. Roentgen., 71: 279–293, 1954.
3. ——, Calvo, W. G., Yamamoto, Y. L., Stickley, E. E., Haymaker, W., and Lippincott, S. W.: Tolerance of central nervous system in man to thermal neutrons. *In* Response of the Nervous System to Ionizing Radiation. T. J. Haley and R. S. Snider, Eds., pp. 441–458. Academic Press, New York, 1962.
4. Sweet, W. H., and Javid, M.: Possible use of neutron-capturing isotopes such as boron-10 in the treatment of neoplasms. 1. Intracranial tumors. J. Neurosurg., 9: 200–209, 1952.
5. Javid, M., Brownell, G. L., and Sweet, W. H.: Possible use of neutron-capturing isotopes such as boron-10 in the treatment of neoplasms. II. Computation of the radiation energies and estimates of effects in normal and neoplastic brain. J. Clin. Invest., 31: 604–610, 1952.
6. Godwin, J. T., Farr, L. E., Sweet, W. H., and Robertson, J. S.: Pathologic study of eight patients with glioblastoma multiforme treated by neutron capture therapy using boron-10. Cancer, 8: 601–615, 1955.
7. Sweet, W. H., Soloway, A. H., and Brownell, G. L.: Studies relevant to slow neutron capture therapy of brain tumor. Acta Union Internationale contre le Cancer, 16: 1212–1219, 1960.
8. Soloway, A. H., Brownell, G. L., Ojemann, R. G., and Sweet, W. H.: Boron-slow neutron capture therapy: Present status. *In* Preparation and Biomedical Application of Labeled Molecules. J. Sirchis, Ed., pp. 383–403. Euratom, Brussels, 1964.
9. Farr, L. E., Haymaker, W., Konikowski, T., and Lippincott, S. W.: Effects of alpha particles randomly induced in the brain in the neutron-capture treatment of intracranial neoplasms. Int. J. Neurol., 3: 564–596, 1962.
10. Locher, G. L.: Biological effects and therapeutic possibilities of neutrons. Am. J. Roentgen., 36: 1–36, 1936.
11. Sweet, W. H.: The uses of nuclear disintegration in the diagnosis and treatment of brain tumor. New Eng. J. Med., 245: 875–878, 1951.
12. Soloway, A. H., De Rougemont, J. G., and Sweet, W. H.: The re-establishment in dogs of the blood-brain barrier to tri-isopropanolamine borate. Neurochir., 3: 1–5, 1960.
13. ——, Wright, R. L., and Messer, J. R.: Evaluation of boron compounds for use in neutron capture therapy of brain tumors. I. Animal investigations. J. Pharmacol. Exper. Therapeut., 134: 117–122, 1961.
14. Sweet, W. H., Soloway, A. H., and Wright, R. L.: Evaluation of boron compounds for use in neutron capture therapy of brain tumors. II. Studies in man. J. Pharmacol. Exper. Therapeut., 137: 263–266, 1962.

instances except two,
characterized by coagul
uefactive chain of eve
ip between radiation
rated topographically

Richardson, Jr. are grateful

capture therapy. Proc. Nucl.

Locksley, H. B., Sutherland,
Neutron capture therapy with
ne. Amer. J. Roentgen., 71:

Haymaker, W., and Lippincott,
man to thermal neutrons. In
ation. T. J. Haley and R. S.
1962.

uring isotopes such as boron
tumors. J. Neurosurg. 9: 200-

le use of neutron-capturing
isms. II. Computation of the
nal and neoplastic brain. J.

, J. S.: Pathologic study of
by neutron capture therapy

ies relevant to slow neutron
tionale contre le Cancer. 16:

Sweet, W. H.: Boron-slow
ion and Biomedical Applica-
3. Euratom, Brussels. 1964.
ott, S. W.: Effects of alpha
n-capture treatment of intra-

ilities of neutrons. Am. J.

nosis and treatment of brain

.: The re-establishment in
nine borate. Neurochir., 3:

oron compounds for use in
nvestigations. J. Pharmacol.

ion of boron compounds for
udies in man. J. Pharmacol.

...ERA, J. M., Thompson, H. G., Jr., and Pool, J. L.: Should we treat glioblastoma multiforme? Amer. J. Roentgen., Rad. Ther., and Nucl. Med., 87: 473–479, 1962.

...AN, W.: Pathogenesis of radiolesions in the mature central nervous system. Proc. 5th International Congress of Neuropathology, pp. 302–308. Zurich, Aug. 31–Sept. 3, 1965.

...LSEN, S. L., Kjellberg, R. N., Asbury, A. K., and Koehler, A. M.: Neuropathological effects of proton beam irradiation in man. Proc. 5th International Congress of Neuropathology, pp. 203–210. Paris, Aug. 31–Sept. 4, 1970.

...YMAKER, W., Laqueur, G., Nauta, W. J. H., Pickering, J. E., Sloper, J. C., and Vogel, F. S.: The effects of barium[140]-lanthanum[140] (gamma) radiation on the central nervous system and pituitary gland of macaque monkeys. J. Neuropath. Exp. Neurol., 17: 12–57, 1958.

Vogel, F. S., Hoak, C. G., Sloper, J. C., and Haymaker, W.: The induction of acute morphological changes in the central nervous system and pituitary body of macaque monkeys by cobalt[60] (gamma) radiation. J. Neuropath. Exp. Neurol., 17: 138–150, 1958.

Haymaker, W.: Effects of ionizing radiation on nervous tissue. *In* The Structure and Function of Nervous Tissue. Vol. III. G. H. Bourne, Ed., pp. 441–518. Academic Press, New York, 1969.

Locksley, H. B., and Sweet, W. H.: Tissue distribution of boron compounds in relation to neutron-capture therapy of cancer. Proc. Soc. Exper. Biol. Med., 86: 56–63, 1954.

Edwards, L. C.: Autoradiography by neutron activation: The cellular distribution of boron-10 in the transplanted mouse brain tumor. Int. J. App. Rad. Isotopes, 1: 81–190, 1956.

Zer..., N. T., and Soloway, A. H.: The microscopic distribution of water soluble compounds by autoradiography. J. Neuropath. Exp. Neurol., 23: 151–155, 1964.

... Terao, H.: Unpublished data. Neurosurgical Research Laboratory, Massachusetts General Hospital.

25. Benda, P., Someda, K., Messer, J., and Sweet, W. H.: Morphological and immunochemical studies of rat glial tumors and clonal stains propogated in culture. J. Neurosurg., 34: 310–323, 1971.

26. Amano, K.: Unpublished data. Neurosurgical Research Laboratory, Massachusetts General Hospital.

MIT 1001947

CERTIFICATE OF SERVICE

The undersigned attorney hereby certifies that the **PLAINTIFF, MASSACHUSETTS INSTITUTE OF TECHNOLOGY'S RESPONSE TO UNITED STATES' MOTION TO DISMISS, IN PART, AND MOTION FOR PARTIAL SUMMARY JUDGMENT** and supporting documents were served upon on counsel of record to this action by mailing a copy of the same, postage prepaid, on this day to:

David W. Ogden
Assistant Attorney General
David M. Cohen
Director
Brian M. Simkin
Senior Trial Counsel
Commercial Litigation Branch
Civil Division
Department of Justice
1101 L. Street, N.W.
Washington, DC 20530
(202) 307-6289

John F. Cordes, Jr.
Marjorie S. Nordlinger
Office of the General Counsel
Nuclear Regulatory Commission
Washington, DC 20555

Edward C. Jiran
Office of the General Counsel
Department of Energy
Washington, DC 20585

Thomas P. Billings
Sally & Fitch
225 Franklin Street
Boston, MA 02110

Date: April 5, 2001 Attorney: ____________________