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● *Original Contribution*

INTRAOPERATIVE RADIATION THERAPY AT THE NATIONAL CANCER INSTITUTE: TECHNICAL INNOVATIONS AND DOSIMETRY

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The technical complexity of intraoperative radiotherapy (IORT) requires modification of the standard physical and dosimetric methods used in external electron beam therapy. At the National Cancer Institute, a number of technical innovations have been integrated into ongoing clinical studies of IORT. These include: (1) an electron beam applicator system that is significantly different from other IORT systems and includes customized "squircle" applicators; (2) peripheral dose shields; (3) a modified surgical table replacing the standard radiation treatment couch; and (4) routine use of multiple IORT fields that necessitates field matching. The IORT applicator system and related devices and techniques are dosimetrically characterized in detail both for use in the IORT program and in order to illustrate many useful facets of electron dosimetry.

Intraoperative radiotherapy, Electron dosimetry, Field matching, Scatter dose.

INTRODUCTION

Intraoperative radiotherapy (IORT) is an innovative treatment modality for locally advanced tumors of the abdomen, pelvis and retroperitoneum where local control is difficult to achieve using surgery alone or combined with high dose external beam irradiation. Basically IORT involves the use of a large single dose of radiation delivered to a tumor or tumor bed and areas of potential regional spread at the time of surgical exploration. IORT may improve the therapeutic ratio of tumor control to normal tissue injury both by (1) direct visualization of the tumor and the consequent precise determination of the tumor volume, and (2) direct appositional treatment which permits exclusion of all or part of a sensitive normal tissue or organ by operative mobilization, customized lead shielding, and/or the selection of appropriate beam energies. Theoretically, these are major advantages when compared to the conventional use of external beam irradiation.

At the National Cancer Institute (NCI), experimental normal tissue tolerance and clinical studies combining surgery and high energy electron beam IORT have been ongoing since 1979, with approximately 100 dogs and 85 patients treated on these studies.[6,7,11–13,15] The technique used for clinical IORT at the NCI differs from other U.S. centers in that higher doses and larger multiple IORT fields are routinely used following gross surgical resection. In this paper, we illustrate several technical innovations, including the electron beam applicator system, a TV verification system, and the use of a modified surgical table as the IORT couch. The complete dosimetry of the IORT system is described in detail.

METHODS AND MATERIALS

Apparatus

The initiation of an IORT program involves the fabrication of many devices. This includes development

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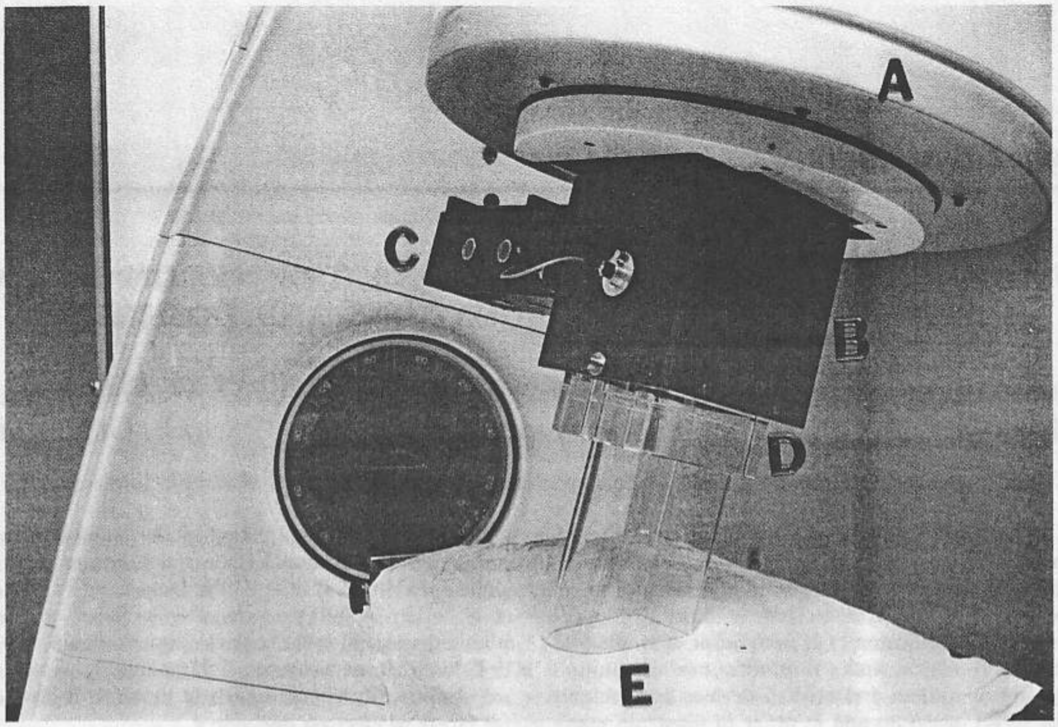

Fig. 1A. IORT applicator system for the Clinac 20. (A) Head of accelerator; (B) IORT adaptor, which attaches to the Clinac 20 head, satisfies all the electron cone interlocks, attenuates the non-useful part of the electron beam, and is used as the mount for the TV system; (C) TV system; (D) Docking adaptor; (E) Beveled squircle applicator.

of an applicator system; adapting that applicator system to the treatment machine; determination of the number, shapes, and sizes of the applicators; and development of a field verification system. The design of the applicators and adaptor system strongly affects the dosimetric properties of the IORT system and must be carefully studied. In this section, the equipment that has been developed for use in IORT is described.

Two linear accelerators have been used for IORT at the NCI; one with 7 and 11 MeV electrons,* and a second wih electron energies from 6 to 20 MeV.† A microtron,‡ with 10 electron energies from 5 to 22 MeV, is now installed in the NCI IORT surgical suite and is in use. All of the devices described in this work are used both with the accelerators and the microtron.

Applicator system

The IORT applicator system consists of a set of applicators, a set of docking adaptors (one for each applicator), and the IORT adaptor. The system is pictured and schematically illustrated in Figure 1. The IORT adaptor is a box that slides into the head of the accelerator, replacing the accessory mount. The adaptor is fitted with a specially coded plug that satisfies all of the electron cone interlocks and allows adjustment of the X ray collimators using two potentiometers mounted on the side of the box. A TV camera and lights, for the TV verification system, mount on the box. The bottom of the adaptor is a sandwich of 1 cm acrylic, 0.6 cm lead, and 5 cm acrylic to attenuate the non-useful part of the electron beam. There is a hole in the center of the adaptor (13 cm × 21 cm), which fits all of the docking adaptors, with a small lip at the top that is a positive stop for the docking adaptors. This hole is covered by a 0.2 mm thick plastic sheet to isolate the sterile operative field from the IORT adaptor and the TV/mirror assembly. Two spring-loaded screws secure the docking adaptor into the IORT adaptor.

The docking adaptors are 10 cm thick acrylic rectangles that fit up into the IORT adaptor. These docking adaptors are gas sterilized along with the treatment applicators, and are considered part of the sterile field during the IORT procedure.

Electron applicators

The design of the IORT applicators has been determined by the areas to be treated and by other technical details of the IORT procedure. All of the IORT electron applicators are fabricated from 0.6 cm thick acrylic, bonded with acrylic solvent where necessary. The length

* Siemens MeVatron XII.

† Varian Clinac 20.

‡ Scanditronix M22 Microtron.

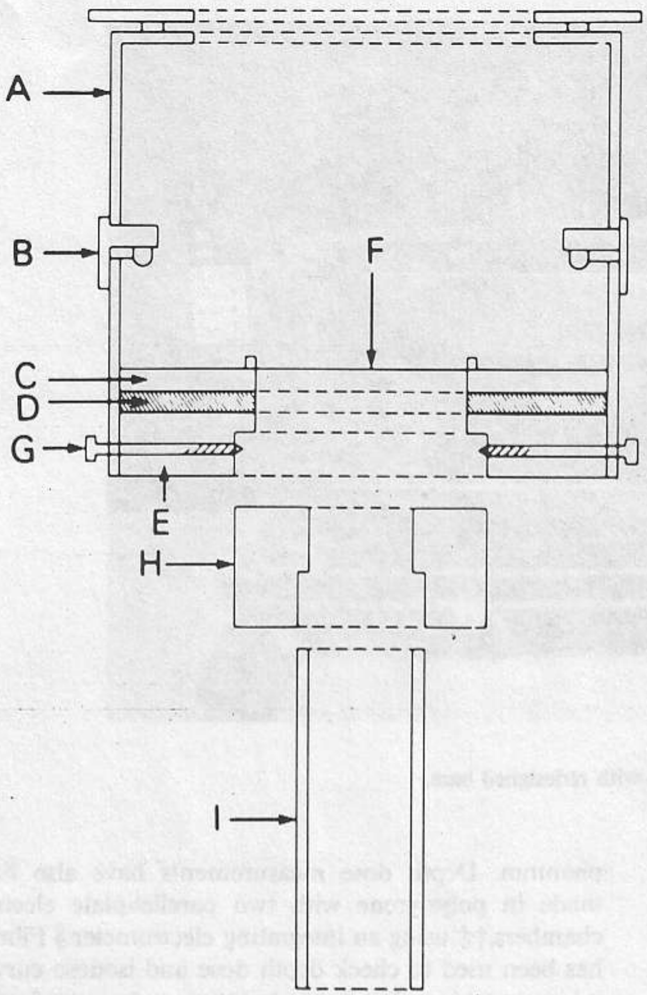

Fig. 1B. IORT applicator system, front view. (A) IORT adaptor, 22 × 22 × 25 cm Al box; (B) TV system lights; (C) 1 cm thick acrylic; (D) 0.6 cm thick lead; (E) 5 cm thick acrylic; (F) 0.2 mm thick mylar sheet to isolate patient from applicator equipment; (G) Spring-loaded screws for securing docking adaptor; (H) Docking adaptor, 10 cm thick acrylic; (I) Applicator, 0.6 cm acrylic walls.

of the applicators is set so that the end of the applicator is 105 cm from the target of the accelerator (5 cm longer than the isocentric distance, in order to have more room to manuever inside the patient). The applicators extend 6 cm up inside the docking adaptor when at the normal treatment distance, although the applicator is free to move up and down inside the adaptor for the safety of the patient. After docking, an etched line on the applicator is even with the bottom of the docking adaptor.

"Squircle-shaped" applicators (Figure 1) are used most often, particularly in the upper abdomen and pelvis. The squircle applicator has one square and one circular end. It is beveled at an angle of 15 degrees, so that the circular end of the applicator is longer than the square end. The beveled, circular character of the applicator allows for easy use on sloping surfaces such as the pelvic side wall. The square end is important because nearly all fields will be matched to another IORT field, and the square end of the applicator greatly facilitates the field matching.

The number of applicators fabricated for IORT use at the NCI has been much fewer than that at other institutions.[9] In our clinical studies, multiple (usually 2–4) fields are used to encompass the tumor volume adequately. The most commonly used applicators are four beveled (15 degree) "squircle" applicators with dimensions 6 × 6, 9 × 9, 9 × 12, and 9 × 15 cm. Rectangular applicators (9 × 12 and 10 × 17 cm) are also available. For the normal-tissue-tolerance dog studies, circular applicators (5 cm diameter with no bevel and 9 cm diameter with a 25 degree bevel) are used.

An important addition to the IORT procedure has been the use of a stainless steel shield around the applicator when it is placed in the patient. This shield has two functions. The primary purpose is to decrease the peripheral dose (the dose outside the radiation field) to normal structures. The shield also acts as a retractor of normal tissues. The shields are 15 cm long, 1.6 mm thick, and are fitted to slide easily over the acrylic applicators. The effect of the shield on the dose distribution is described below.

Television verification and documentation system

Verification of the area to be treated with IORT before treatment and accurate documentation of the area that has been treated are crucial if IORT is to be used effectively and the results are to be assessed accurately. We have developed a television system that allows both of the above tasks to be easily performed. As previously described,[4] a TV camera is mounted to the side of the IORT adaptor (Figure 1). A mirror slides in and out of the adaptor box, allowing the TV camera to look down on the area to be treated. During the docking procedure (docking the applicator into the adaptor, which is fixed in the head of the accelerator) and immediately before and after irradiation, the surgeon and therapist view the area to be treated on a large TV monitor. The whole procedure is recorded with a video cassette recorder and hard copy pictures can be made for inclusion into the patient's chart.

IORT table

Surgical tables generally have no provision for the fine vertical, lateral, and longitudinal motions that are crucial to the IORT docking procedure. Radiotherapy couches, which do have the above capabilities, are flat and do not tilt, making many surgical approaches impossible. Therefore, we have designed and built a base for a normal surgical table§ (Figure 2), which has the following features:

§ AAMSCO Surgical 2080 RC.

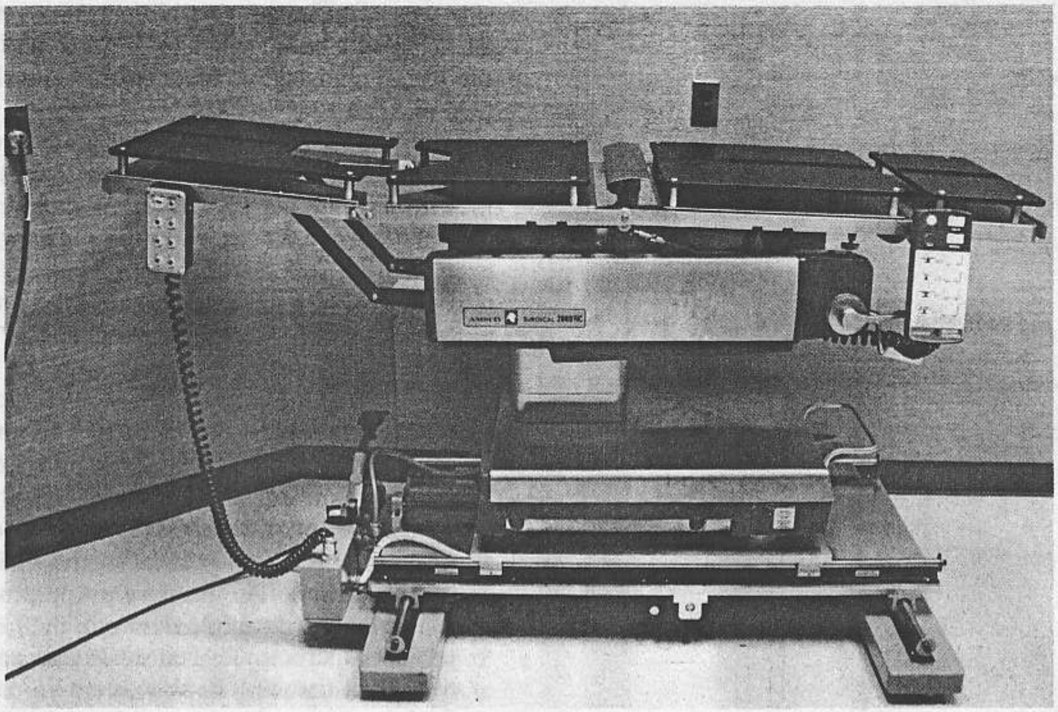

Fig. 2. IORT table with redesigned base.

1. casters to allow rough table positioning under the accelerator, and hydraulic pads, which fix the table in the desired spot,
2. electrical lateral and longitudinal drives, which enable fine positioning during docking,
3. modification of the vertical (electro-hydraulic) motion of the table so that the upward motion is slow (for docking), and the downward motion is fast.

The base modification increases the height of the surgical table by only 23 cm. The surgical motions, especially the Trendellenburg motion, have been very important in speeding up otherwise very difficult docking for many IORT cases.

Measurement technique

The majority of the dosimetry data have been obtained from measurements using diodes or 0.1 cc ionization chambers in the ratio circuit of an automated scanning water phantom system.* For these measurements, an LSI-11 computer controls the positioning and dose measurements from the water phantom system.[3] Several types of film and ionization measurements have been made to check the validity of the diode data. Integration ionization chamber measurements have been made with a 0.2 cc Baldwin-Farmer ion chamber in the water phantom. Depth dose measurements have also been made in polystyrene with two parellel-plate electron chambers,†‡ using an integrating electrometer.§ Film** has been used to check depth dose and isodose curves; it is exposed in polystyrene phantoms and scanned using an automated film densitometer*, with the readings corrected from optical density to dose using measured calibration curves.

A comparison of the depth dose from a 20 MeV electron field obtained with different measurement techniques (Figure 3) is indicative of the data for energies from 12 to 20 MeV. The agreement between the data measured with the diodes, the corrected ionization data and the corrected film data allows most of the dosimetric data required for the characterization of the IORT system to be obtained with the diodes in a water phantom. The major exception, especially for IORT, is the measurement of the surface dose. A thin window, parallel-plate ionization chamber must be used for these measurements, since the dose to the surface of the tumor bed must be accurately known.

DOSIMETRIC RESULTS

The IORT applicator system developed at the NCI is significantly different from those used at other institu-

* Theradros RFA-3.
† Nuclear Associates 30-404 Parallel Plate Ion Chamber.
‡ Capintec PS-033 Thin Window Parallel Plate Ion Chamber.
§ Keithley 616/6169 Electrometer.
** Kodak RPV Film.

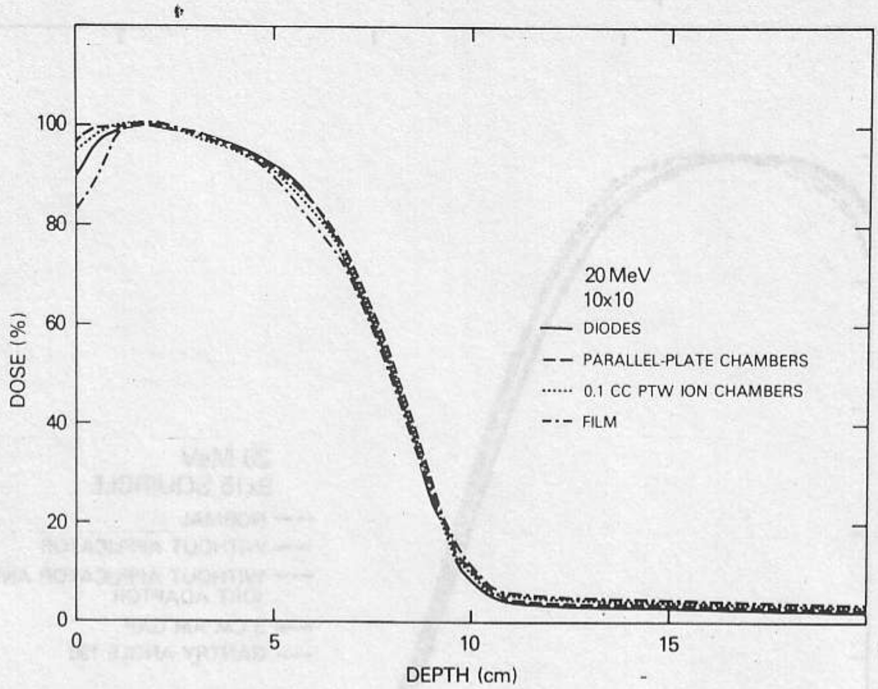

Fig. 3. Percent depth dose for 20 MeV electrons, 10 × 10 cm cone, at 100 cm SSD. Data from diodes, ion chamber, and film in water or polystyrene are shown.

tions.[2,9] The collimation of the electron is determined by the several pieces of the applicator system, including the applicator, the docking adaptor, the IORT adaptor, and the X ray jaws of the accelerator. The effect of each of these pieces on field flatness, depth dose, X ray contamination, and peripheral dose has been measured and analyzed. All of the dosimetric data presented here have been obtained with the 20 MeV accelerator, although they are also representative of the data from the microtron.

Depth dose

The depth dose from high energy electron fields is affected by a variety of different factors. The extent of the collimation clearly affects the shape of the depth dose curve as illustrated in Figure 4. The presence of the applicator increases the surface dose, moves the depth of maximum dose (dmax) closer to the surface, and makes the deep part of the curve less steep. The presence of other components in the applicator system does not have significant effect. A gap between the end of the applicator and the surface of the phantom is easy to investigate, since the applicator freely slides inside its adaptor. As shown in Figure 4, the only effect of a 3 cm air gap on the central ray depth dose is a slight decrease in the surface dose.

Electron applicators with beveled ends are very useful in IORT. Biggs (1) has studied the effects of beam angulations to 60 degrees with respect to normal incidence for energies up to 29 MeV, and has shown that there are significant changes in the depth of dmax and the steepness of the descending part of the depth dose curve, as the angle increases and the energy decreases. The relationship of the field size to the electron energy (or the average range of the scattered electrons) is of great importance. The effect of bevel angle on the depth dose in our system is illustrated by comparing the usual (15 degrees bevel angle) depth dose with the depth dose produced at a gantry angle of 180 degrees (Figure 4). For our IORT system, the field sizes are large enough and the bevel angles small enough that oblique incidence of the electron beams is not a significant problem.

Electron depth doses can be influenced significantly by varying the setting of the X ray collimators. For small applicator sizes with respect to the range of the electrons, the depth dose changes little as the jaw setting is changed from 5 × 5 to 35 × 35 cm, as illustrated in Figure 5A. This is the range on which most other reports of IORT applicator systems have concentrated.[2,9] However, when the fields are large, the depth dose is affected (Figure 5B). As the X ray jaws for the 10 × 17 cm applicator are opened from 10 × 17 to 35 × 35 cm, the surface dose increases slightly, and the slope of the deep part of the curve decreases significantly. For 20 MeV, the depth of the 90% line moves toward the surface by more than one centimeter. The X ray jaw setting also affects the field flatness. Therefore, one must carefully consider the possible trade-offs when designing and defining the collimation system. For example, the surface dose is decreased when the X ray jaw sizes are decreased. On the other hand, measurements with the thin window, parallel-plate ion chamber show that the surface dose is

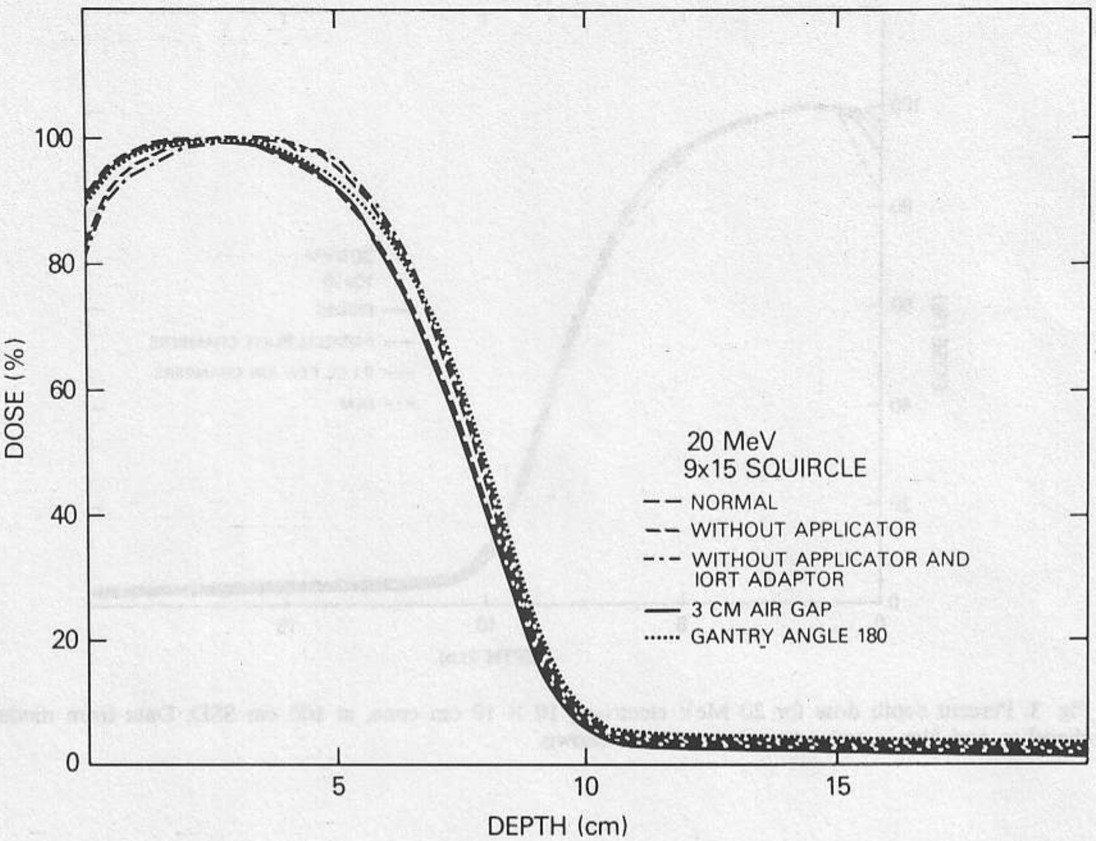

Fig. 4. Depth dose curves for the 9 × 15 cm squircle applicator at 20 MeV.

greater than 90% of the maximum for all the applicator and energy combinations used at the NCI for clinical IORT.

Beam profiles

The shapes of the isodose charts and cross-beam profiles from the IORT applicators are influenced both by the design of the applicator system and the setting of the X ray jaws which are used with each applicator. These effects are complicated by the beveled applicators and non-standard applicator shapes which are used for IORT. Figure 6 shows several cross beam profiles for the 9 × 15 cm "squircle" applicator (15 degree bevel) at a depth of dmax. The applicator itself is responsible for most of the electron collimation not performed by the X ray jaws, which are set for a 9.5 × 15 cm field. Also illustrated is the effect of a 3 cm air gap between the end of the applicator and the phantom surface: the air gap decreases the "horns" near the edges of the applicator which are almost unavoidable in the IORT setting, since the applicator must extend all the way to the surface of the areas to be irradiated. The final effect illustrated is that of non-normal incidence of the electrons. Changing the gantry angle so that the electron beam enters normal to the phantom surface significantly decreases the flatness of the electron beam from the "squircle" applicator.

The setting of the X ray collimator has a large effect on the flatness of the dose profiles for all electron applicators, especially for IORT applicators. Figure 7 illustrates the effect of changing the X ray jaw setting on the beam profiles for the 10 × 17 cm applicator. The horns that result from scattering from the end of the applicator as it sits on the phantom surface may be reduced simply by decreasing the X ray jaw size. X ray collimator settings are thus chosen so that the cross-beam profile at a depth of dmax has horns of 2 to 4% above the dose at dmax on the central axis of the field. It should be noted that the choice of jaw size is tempered by the following considerations: (1) the depth dose is changed by the jaw size, as illustrated above; (2) the output factor (cGy/MU) can become unacceptably low for small applicators with small X ray jaw sizes, as has been previously noted.[2] This problem is easily rectified, however, since changing the jaw sizes from 5 × 5 to 10 × 10 for the 5 cm diameter applicator increases the output factor dramatically while changing the field flatness by only 2% for 12 MeV electrons. The change in flatness gets much larger as the energy increases, however, so that we do not use the 5 cm applicator at energies

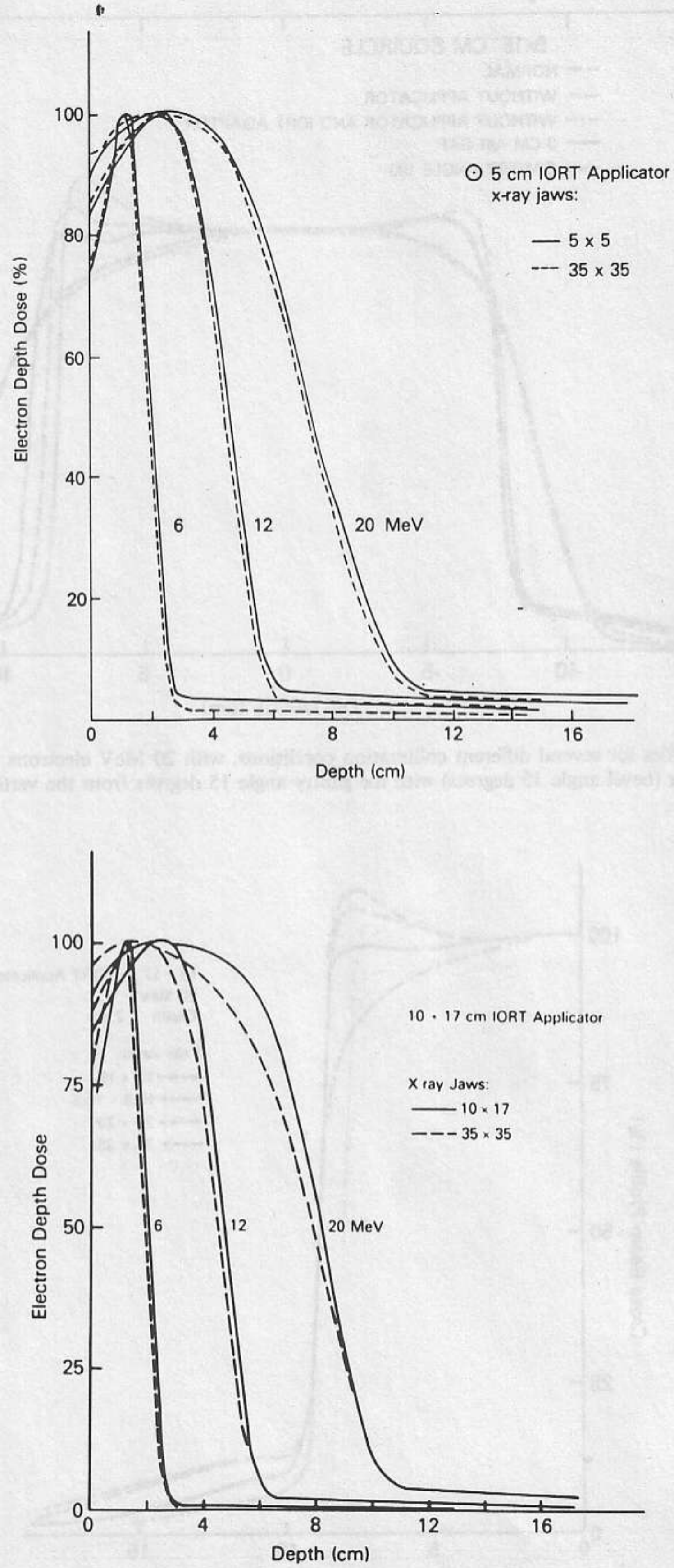

Fig. 5. Percent depth dose variation with X ray jaw setting for 6, 12, and 20 MeV electrons. (A) 5 cm diameter cylindrical applicator; (B) 10 × 17 cm rectangular applicator.

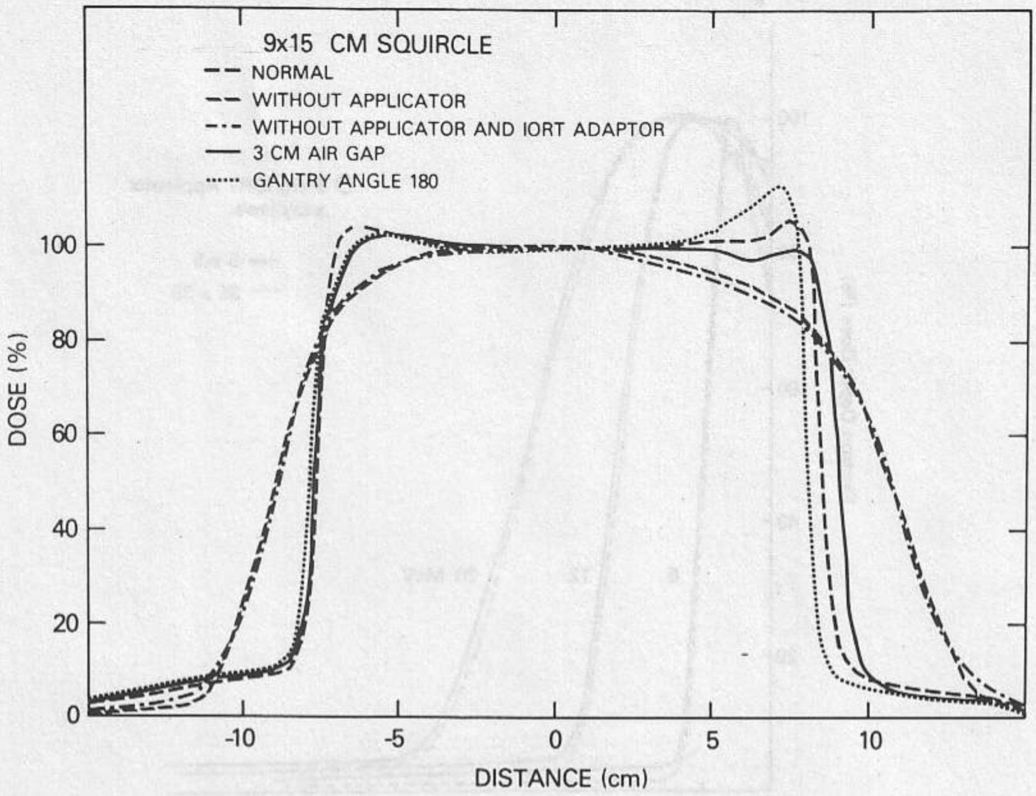

Fig. 6. Beam profiles for several different collimation conditions, with 20 MeV electrons using the 9 × 15 cm squircle applicator (bevel angle 15 degrees) with the gantry angle 15 degrees from the vertical.

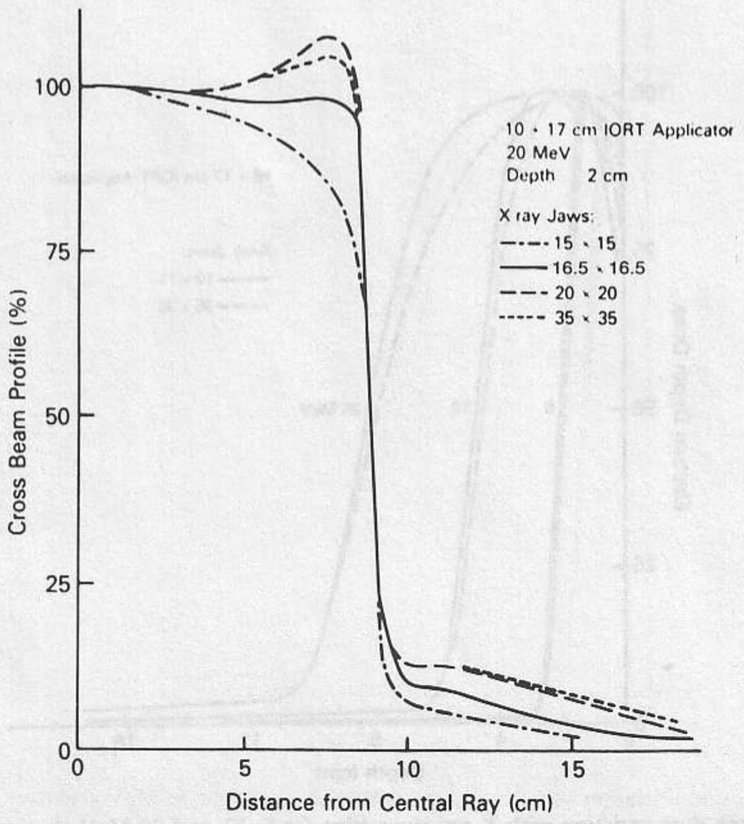

Fig. 7. Cross plots at 2 cm depth (dmax) for 10 × 17 cm applicator, 20 MeV electrons, for different X ray jaw settings.

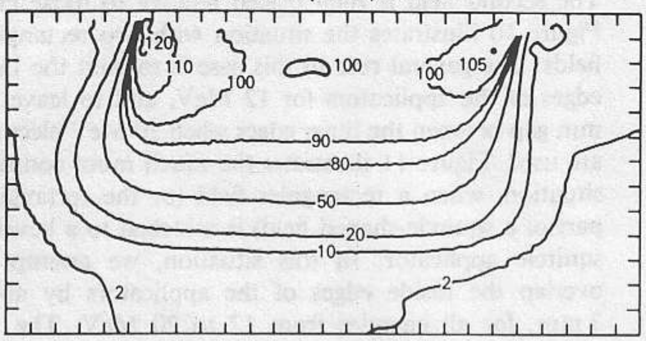

Fig. 8. Isodose chart for the 9 × 15 cm squircle applicator, 20 MeV electrons.

greater than 12 MeV. The output factors (cGy/MU relative to the standard 10 × 10 cm cone at 100 SSD and depth of dmax) vary from 0.80 to 0.91 for the applicators and energies (12 to 20 MeV) used clinically for IORT.

Figure 8 shows the isodose chart obtained with 20 MeV electrons for the 9 × 15 cm "squircle" IORT applicator (15 degree bevel), illustrating the success of the applicator design. The dose is prescribed to the 90% line for our IORT cases, and this figure shows the uniformity of the 90% line, even for areas as large as 17 cm and for the squircle-bevel situation. The hot spots near the applicator edges have been minimized by adjusting the X ray jaw setting for each energy and applicator. This also increases the depth of the 80% and 90% dose lines, as seen in Figure 5B. Although the surface dose is decreased through this procedure, it is still greater than 90% of the maximum dose for all our clinical applicators and energies.

Peripheral dose

The dose outside the radiation field (the "peripheral dose") is important in IORT, especially at the NCI where the IORT dose may be as high as 30 Gy for patients and 70 Gy for normal-tissue tolerance dog studies. Peripheral doses of 10%[2] and as much as 30%[9] have been reported in the literature. We have decreased the peripheral dose to approximately 2% of the dose inside the field.

The peripheral dose decrease has been accomplished in two ways. The first is through effective design of the applicator system. The base plate of the IORT adaptor is a sandwich of 6 cm of acrylic and 0.6 cm of lead, which is sufficient to stop 20 MeV electrons. The docking adaptors are 10 cm thick acrylic, also thick enough to stop any incident electrons. There are no vertical joints directly open to electrons, and the tolerances of the joints are only 0.1 mm. The choice of X ray jaw setting also appreciably decreases the flux of electrons incident on this part of the applicator system.

An additional decrease of the peripheral dose directly outside the applicator can be obtained through the use of a shield around the applicator, as illustrated in Figure 9. We have fashioned a shield for each applicator from 1.6 mm thick stainless steel. These shields, which can be sterilized, decrease the dose immediately outside the applicator by a factor of five. The shield, however, scatters electrons back into the treatment field, thereby increasing the "horns" on cross beam profiles. X ray

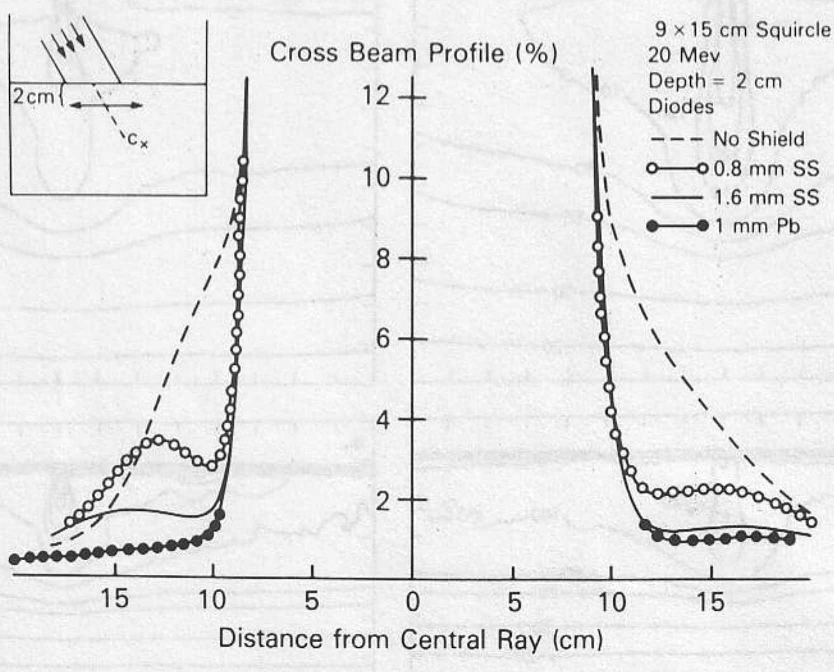

Fig. 9. Peripheral dose shielding. Cross plots for the 9 × 15 cm squircle applicator are shown at 2 cm depth for 20 MeV electrons with several types of shields.

jaw settings must thus be determined with the shield in place.

Field matching

Nearly every IORT procedure at the NCI involves the use of multiple radiation fields. Proper matching of these electron fields is critical. Although methods for improved matching of electron fields have been proposed for use in the already difficult situation of electron fields matched at the surface of the patient,[5,14] application of these techniques in the special setting of IORT is difficult. Therefore, we have determined rules that allow adequate field matching for various clinical IORT situations.

The first field edge is marked by implanting surgical clips in the tissue on the inside edge of the applicator. The second field is then placed relative to those clips. Figure 10 illustrates the situation with two rectangular fields. The general rule in this case is to abut the inner edges of the applicators for 12 MeV, and to leave a 2 mm gap between the inner edges when 20 MeV electrons are used. Figure 11 illustrates the much more common situation, when a rectangular field (or the rectangular part of a squircle-shaped field) is matched to a beveled, squircle applicator. In this situation, we attempt to overlap the inside edges of the applicators by about 3 mm, for all energies from 12 to 20 MeV. The TV verification system is essential for field matching, since it allows visualization of the relationship of the new field edge with respect to the clips which delineate the first field. The field matching procedure is by no means easy or exact. However, with careful attention to detail,

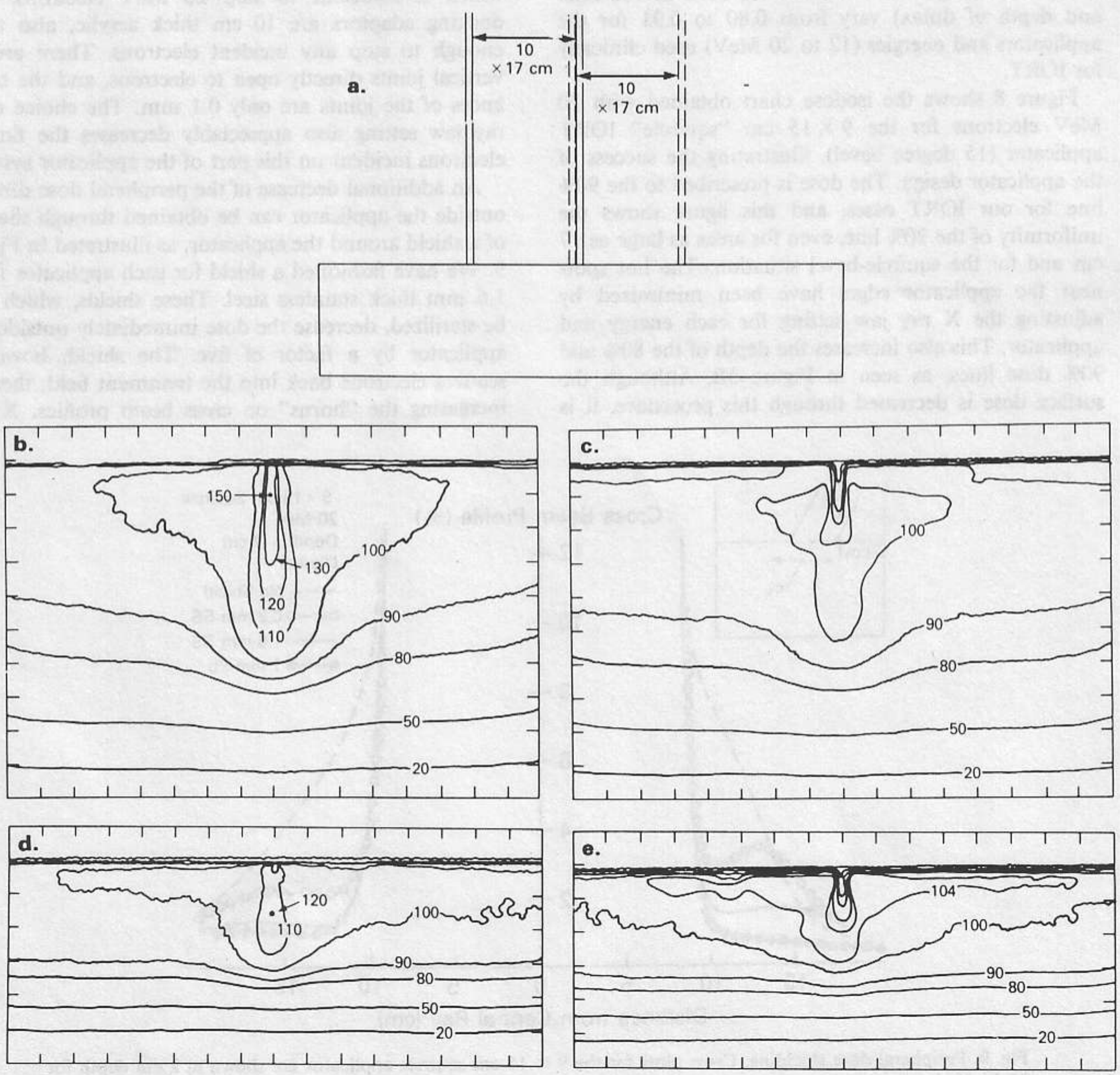

Fig. 10. Matching two 10 × 17 cm fields side by side. (A) Geometry. (B) 20 MeV, inside edges abutted. (C) 20 MeV, 2 mm gap. (D) 12 MeV, inside edges abutted. (E) 12 MeV, 5 mm gap. Film data.

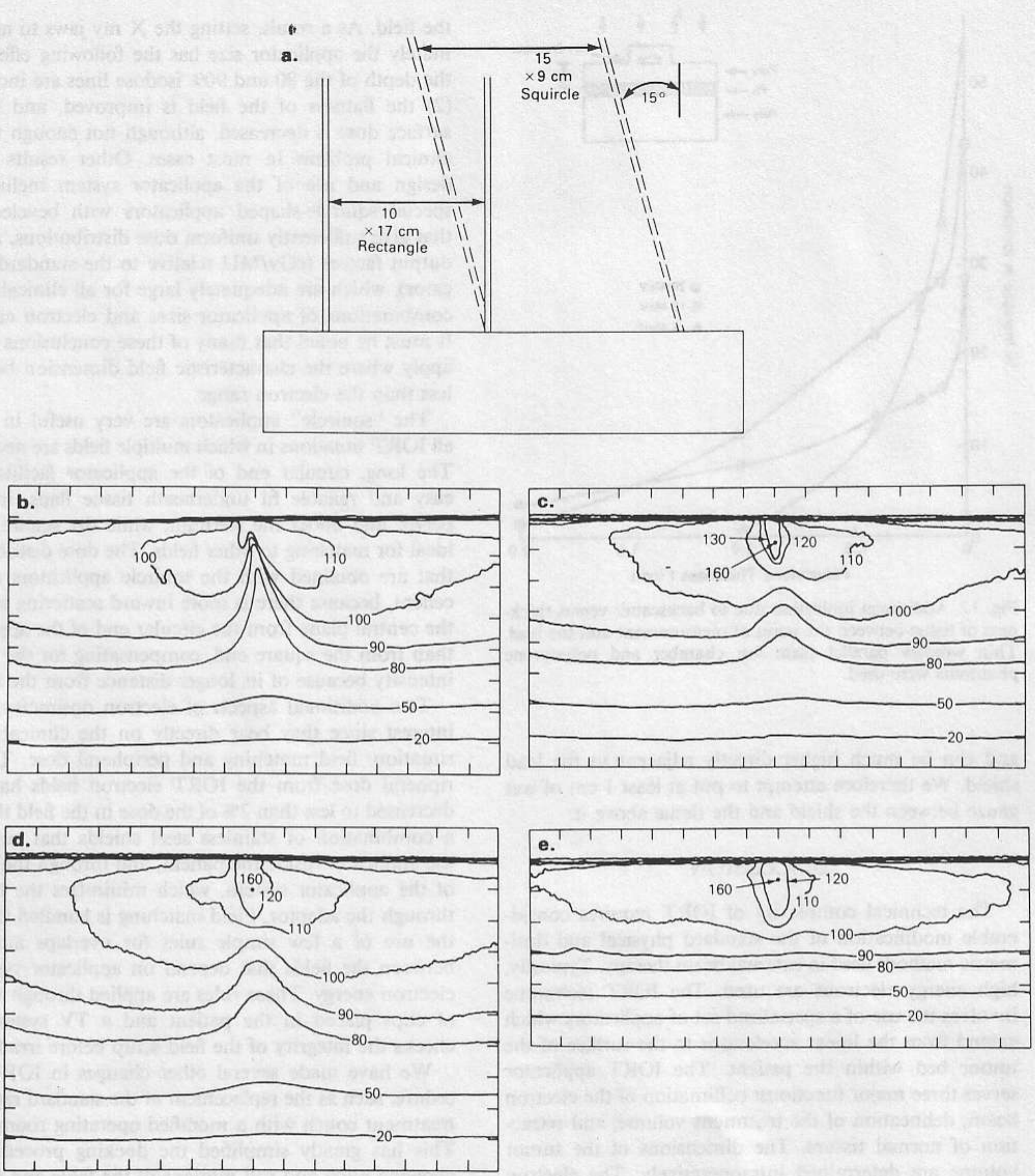

Fig. 11. Matching the 10 × 17 cm rectangle to the 9 × 15 cm squircle (beveled). (A) Geometry; (B) 16 MeV, inside edges abutted; (C) 16 MeV, 3 mm overlap; (D) 20 MeV, 3 mm overlap; (E) 12 MeV, 3 mm overlap. Film data.

there has been no clinical evidence of any problems due to field matching in the 85 patients treated with these techniques.

Backscatter

One of the arguments in favor of the use of IORT is that it is possible to mobilize normal structures surgically and remove them or shield them from the radiation. One method used may be to manipulate the tissues surgically so that a lead shield may be placed behind one structure, shielding another. In this setting, the backscatter from the lead shield must be included in the dose calculations. The magnitude of the backscatter is shown in Figure 12 for a simple set of experiments using the thin window parallel-plate chamber. These data, which are in essential agreement with previously published work,[8,10] show that the magnitude of the effect is between 10% and 30% for 12 to 20 MeV electrons

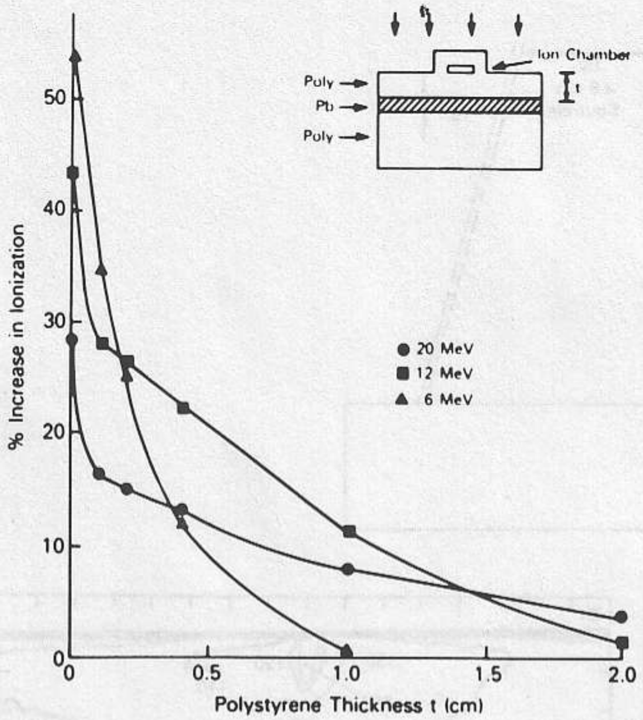

Fig. 12. Additional ionization due to backscatter versus thickness of tissue between the point of measurement and the lead. Thin window parallel plate ion chamber and polystyrene phantoms were used.

and can be much higher directly adjacent to the lead shield. We therefore attempt to put at least 1 cm of wet gauze between the shield and the tissue above it.

DISCUSSION

The technical complexity of IORT requires considerable modification of the standard physical and dosimetric methods used in external beam therapy. Typically, high energy electrons are used. The IORT technique involves the use of a specialized set of applicators which extend from the linear accelerator to the surface of the tumor bed within the patient. The IORT applicator serves three major functions: collimation of the electron beam; delineation of the treatment volume; and retraction of normal tissues. The dimensions of the tumor volume are determined intraoperatively. The electron applicators which are selected must both encompass the tumor volume and adapt to the patient's anatomy. With large tumor volumes, two or more IORT fields may be used, necessitating field matching. A complete set of isodose curves should be available for each electron adaptor for each electron energy to facilitate selection of the applicators during surgery.

The dosimetry of the IORT apparatus described in the present work is significantly different from that of the other IORT systems because the physical parameters are different. At the NCI, the treatment fields are usually large compared to the range of electrons scattered from the field. As a result, setting the X ray jaws to approximately the applicator size has the following effects: (1) the depth of the 80 and 90% isodose lines are increased, (2) the flatness of the field is improved, and (3) the surface dose is decreased, although not enough to be a clinical problem in most cases. Other results of the design and use of the applicator system include: (4) special squircle-shaped applicators with beveled ends that give sufficiently uniform dose distributions, and (5) output factors (cGy/MU relative to the standard applicator), which are adequately large for all clinically-used combinations of applicator sizes and electron energies. It must be noted that many of these conclusions do not apply where the characteristic field dimension becomes less than the electron range.

The "squircle" applicators are very useful in nearly all IORT situations in which multiple fields are necessary. The long, circular end of the applicator facilitates an easy and reliable fit underneath tissue flaps, into the pelvis, and under the sternum, while the square end is ideal for matching to other fields. The dose distributions that are obtained with the squircle applicators are excellent, because there is more inward scattering towards the central plane from the circular end of the applicator than from the square end, compensating for the loss of intensity because of its longer distance from the source.

Two additional aspects of electron dosimetry are of interest since they bear directly on the clinical IORT situation: field matching and peripheral dose. The peripheral dose from the IORT electron fields has been decreased to less than 2% of the dose in the field through a combination of stainless steel shields that surround the applicator inside the patient, and through the design of the applicator system, which minimizes the leakage through the adaptor. Field matching is handled through the use of a few simple rules for overlaps and gaps between the fields that depend on applicator type and electron energy. These rules are applied through the use of clips placed in the patient and a TV system that checks the integrity of the field setup before irradiation.

We have made several other changes in IORT procedure, such as the replacement of the standard radiation treatment couch with a modified operating room table. This has greatly simplified the docking procedure by allowing pitch and roll motions of the table and patient as well as longitudinal, lateral and vertical movements. The ability to adjust the table along multiple axes permits rapid and accurate alignment between the applicator and accelerator for most applicator positions within the body cavities.

The clinical use of IORT remains an experimental treatment. At present, several U.S. centers are involved in clinical studies and a number of other centers are planning to use IORT in the near future. A working group funded by the Radiation Research Program of the NCI, which includes five groups experienced with IORT, is now compiling data on approximately 300 patients to serve as the basis for clinical guidelines in future IORT studies. Further comparison of treatment techniques and equipment, such as those presented in this work, will assist in the standardization of treatment techniques that will be important if IORT is to gain wide acceptance.

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