CHRT

ISSUE BRIEF

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Intensity-Modulated Radiation Therapy for Breast and Lung Cancer: A Review of Use, Cost, Clinical Evidence, and Safety

Intensity-Modulated Radiation Therapy (IMRT) is a type of radiation therapy that uses inverse-planning tools to derive beamlets with variable intensities within each beam to deliver highly conformal radiation doses to tumors while reducing radiation doses to healthy tissues. Its ability to reduce the radiation dose to surrounding tissue means that higher doses can be given to tumors without increasing the dose to healthy tissue. Further, IMRT treatment relies less on the skills of the technicians by essentially eliminating the effect of their skill levels on treatment. Because of this potential benefit, IMRT has been used to treat many different types of cancer.

However, IMRT also introduces new safety and quality concerns. IMRT is an area of particular concern because it is more complex than previous technologies used to administer radiation therapy. It requires sophisticated equipment and software, and staff must be trained on the systems. For staff performing this treatment, a major difference is a loss of intuitively monitoring the treatment because of the involvement of highly advanced technologies. These complexities introduce opportunities for error that did not exist with older technologies.

This issue brief will summarize available data and literature on the use of IMRT for breast and lung cancer—two cancers for which IMRT is emerging as a treatment option. The brief will discuss: (1) trends in IMRT use overall and for breast and lung cancer, (2) the clinical evidence supporting the use of IMRT for breast and lung cancer and (3) safety regulations in Michigan for radiation therapy and IMRT and (4) a review of the evidence related to improving patient safety in radiation therapy.

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Trends in IMRT Use

The first IMRT treatment was delivered in 1995[1], and use of the technology has increased rapidly in the past decade. A 2004 survey by Mell and colleagues[2] found that 73.2 percent of radiation oncologists used IMRT in 2004, compared to only 32 percent in 2002. The top reasons radiation oncologists gave for adopting IMRT were to spare normal tissue/optimize conventional dose delivery (88.0 percent), escalate dose (85.1 percent), and to remain competitive or gain a competitive advantage among other centers (48.9 percent).

In Michigan, 34 percent of all radiation therapy treatments were IMRT in 2009. The percentage of total treatments that were IMRT varied significantly by facility, from a low of 11 percent to a high of 69 percent.[3] Currently, IMRT is being used most extensively to treat head and neck and prostate cancers.[4]

IMRT has also been applied to breast and lung cancers. In an analysis of Blue Cross Blue Shield of Michigan claims data from 2008, 10.6 percent of patients with breast cancer and 9.1 percent of patients with lung cancer were treated with IMRT. FIGURE 1 The use of IMRT is rapidly increasing in lung cancer. Between 2007 and 2008, the number of IMRT services for lung cancer increased by 38.4 percent.

FIGURE: 1
Breast and Lung CRT and IMRT Facilities and Rates of IMRT Use in Michigan, 2008

Breast Cancer	
# of facilities performing 3D CRT	65
# of facilities performing IMRT	20
% of all patients receiving IMRT	10.6%
Range of % of patients receiving IMRT at facilities that administer IMRT	7.1% to 50.0%

Lung Cancer	
# of facilities performing 3D CRT	75
# of facilities performing IMRT	29
% of all patients receiving IMRT	9.1%
Range of % of patients receiving IMRT at facilities that administer IMRT	2.9% to 100%

Source: Blue Cross Blue Shield of Michigan Claims Data

The claims data show substantial variation by facility in the percentage of patients who receive IMRT for breast and lung cancer. For breast cancer, the percentage of patients treated with IMRT ranged from a low of 7.1 percent to a high of 50 percent. Figure 2 For lung cancer, the range was from a low of 2.9 percent to a high of 100 percent. Figure 3

IMRT Costs

IMRT costs substantially more than traditional radiation therapy. In 2008, the average cost of IMRT treatment for breast cancer was $19,388, compared to $4,104 for 3D conformal radiotherapy (3D CRT), or almost five times more expensive. For lung cancer, IMRT cost $13,498 while 3D CRT cost $3,747.[5]

Driving this difference in cost is the increased complexity of delivering IMRT compared to traditional radiation therapy. The planning process is more labor intensive than traditional radiation therapy, and requires sophisticated software to plan and deliver the treatment. IMRT also requires significant quality control for each patient to ensure the radiation dose is being administered correctly to the target volume. For breast and lung cancer, additional steps are needed to account for respiratory motion that may affect the location of the target volume while treatment is being administered.

Figure:2

Percent of Breast Cancer Patients Treated with IMRT in Michigan, by Facility, 2008

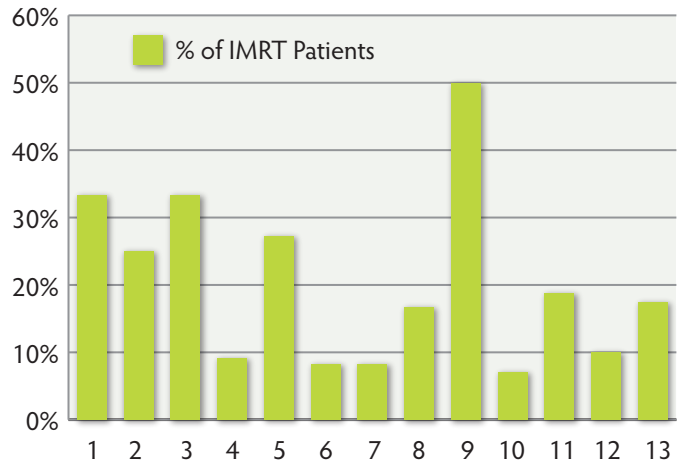
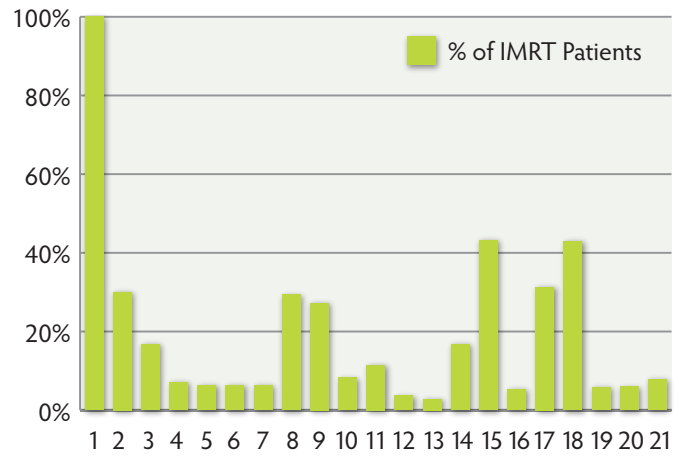


Figure:3

Percent of Lung Cancer Patients Treated with IMRT in Michigan, by Facility, 2008



Source for Figures 2 and 3: Blue Cross Blue Shield of Michigan Claims Data

IMRT Clinical Evidence

IMRT has been extensively studied in dosimetric studies, and has been shown to provide superior dose homogeneity and reduce radiation doses to organs at risk. However, the effect of these dose improvements on outcomes is less well established. The evidence shows reduced toxicity for various tumor sites by use of IMRT. Findings on local control and overall survival are generally inconclusive.[4]

Veldeman et al conducted a systematic review of 49 comparative clinical studies on the use of IMRT. Overall, the ability of IMRT to reduce toxic effects has been shown in three randomized controlled trials—one for head and neck cancer and two for breast cancer. Another 19 comparative studies shows generally favorable outcomes for treatment-related toxicity in head and neck cancer. Sixteen studies on prostate cancer show the ability for dose escalation with the same or lower toxic effects. Thus, the clinical evidence for IMRT in these cancers is well established.

For other types of cancer, there are fewer studies and the studies have generally been small case-study designs. Veldeman identified a single study on lung cancer and four studies on breast cancer. A review of the literature since 2008 identified one additional study on breast cancer and one additional study on lung cancer. Below is a review of the clinical evidence for IMRT in breast and lung cancer treatment. Studies that had a comparison group and examined toxicity-related effects, local control, or survival were included in the analysis.

Clinical Evidence—Breast Cancer

Radiation therapy given after breast conserving surgery or mastectomy significantly reduces the risk of local and regional recurrences and improves overall survival. Traditional radiation therapy for breast cancer uses wedged tangential fields, which can produce inhomogeneous dose distributions, which can lead to skin toxicity and changes in breast appearance. IMRT has been shown to improve dose homogeneity and reduce treatment-induced toxicity in two randomized controlled trials and three retrospective analyses. IMRT and 3D CRT have not been shown to be significantly different in overall survival or local control.

A randomized controlled trial of IMRT versus two dimensional radiotherapy (2D RT) was conducted by Pignol et al.[6] A total of 358 patients were randomly assigned to either IMRT or 2D RT. IMRT was associated with a significantly lower occurrence of moist desquamation during or up to six weeks after treatment; 31.2 percent for IMRT compared with 47.8 percent for standard treatment. IMRT did not correlate with pain or quality of life. IMRT did demonstrate a significantly improved dose distribution compared with the 2D RT technique.

Donovan and colleagues[7] compared IMRT to 2D RT in a randomized controlled trial. The analysis focused on breast appearance, breast discomfort, breast hardness and quality of life. Of 240 women randomized to treatment, 122 received 2D RT and 118 received IMRT. Women who received IMRT had a 40 percent rate of breast appearance changes, while 58 percent of the 2D RT group experienced breast appearance changes. There were no differences in breast discomfort, breast hardness, or quality of life.

Another randomized controlled trial has published results showing improved dose distributions, but final results have not been published yet.[8]

IMRT for breast cancer has also been demonstrated to reduce treatment-related toxicity in three retrospective studies. In the longest follow-up period of the five studies, McDonald et al[9] analyzed long-term outcomes in 121 women who received IMRT and 124 women who received 3D CRT for stages 0–III breast cancer between 1999 and 2003. IMRT treatment reduced Stages 2 and 3 acute skin toxicity compared with 3D CRT; 39 percent for IMRT compared to 52 percent for 3D CRT, $p=0.047$. Comparing IMRT with 3D CRT, there were no statistically significant differences in overall survival, disease-specific survival, tumor recurrence, distant metastasis, late toxicity, or second malignancies.

Freedman et al[10] compared 399 patients treated with IMRT to 405 patients treated with conventional 2D RT. They compared the incidence of acute dermatitis between the groups. Fifty-two percent of patients treated with IMRT experienced Grade 2 or 3 acute dermatitis, compared to 75 percent of patients treated with 2D RT. This analysis found an effect for women of all breast sizes; an earlier analysis by the same authors found that this effect was significant in patients with small and large breasts, but not in those with medium breasts.[11]

Harsolia et al[12] compared 93 patients treated with IMRT to 79 patients treated with 2D RT. A significant reduction in Grade 2 or higher dermatitis, edema, and hyperpigmentation was seen in the IMRT group. No significant difference in cosmesis was observed.

Clinical Evidence—Lung Cancer

Radiation therapy is an important part of the treatment of non-small cell lung cancer, and dose escalation has shown to be effective in improving locoregional control.[14] However, dose escalation is often difficult due to treatment-related complications that result from higher doses of radiation to healthy lung tissue. IMRT is one possible method for achieving dose escalation while sparing healthy tissue.

Two comparative studies have examined the use of IMRT for lung cancer. Both studies showed decreased incidence of radiation pneumonitis in patients treated with IMRT, and one showed an increase in overall survival for patients treated with IMRT.

In a retrospective study, Liao et al[13] examined 91 patients with locally advanced non-small cell lung cancer treated with IMRT and compared them to 318 patients who had received 3D CRT. They compared locoregional progression, distant metastases, overall survival, and toxicity in the two groups. The IMRT group showed a statistically significant advantage in overall survival (Hazard Ratio=0.64, p=0.039). The IMRT group also experienced a lower rate of Grade 3 or higher pneumonitis. Locoregional progression and distant metastases were the same in both groups. Follow-up time for the IMRT group was an average of 1.3 years, compared to 2.1 years in the 3D CRT group. Despite this shorter follow-up time, IMRT appears to be associated with a therapeutic gain, as shown by increased overall survival and decreased toxicity.

Yom and colleagues[14] compared the rate of treatment-related pneumonitis for 155 patients who received IMRT with 222 patients who received 3D CRT. Patients who received IMRT had a significantly lower rate of Grade 3 or higher pneumonitis at 12 months than the 3D CRT group (8 percent vs. 32 percent, respectively).

Summary

IMRT shows promise in reducing treatment-related toxicity for breast and lung cancer. Most significantly, IMRT shows a benefit in overall survival for lung cancer patients in one observational study. It also is associated with lower rates of radiation pneumonitis compared with 3D CRT. For breast cancer, IMRT has been shown in randomized controlled trials to decrease acute skin toxicity and late changes in breast appearance compared to 2D RT. These trials confirm the earlier observational evidence that IMRT is associated with lower rates of treatment-related toxicity for breast cancer. When compared to 3D CRT, IMRT has been shown to reduce skin toxicity in one observational trial. More research is needed to better understand the benefits and risks of IMRT compared to 3D CRT, the current standard of care for breast cancer patients.

Given the rapid increase in the use of and the substantial additional cost for IMRT, prospective studies are needed to confirm the survival benefit of IMRT for lung cancer. In addition, further study is needed to determine which patients are most likely to benefit from IMRT.

IMRT Safety and Regulation

Due to the rapidly increasing use of IMRT, and the complexity of IMRT treatment planning and administration, patient safety has become an increasing concern. Because the radiation beams used in IMRT are so highly targeted, a small error in placement or dose can irradiate the healthy and vulnerable tissues IMRT is designed to protect.

In January 2010, the New York Times published an article highlighting errors that have occurred in radiation therapy, with a focus on IMRT. This analysis showed that catastrophic preventable errors still occur in New York, despite the state being one of the most stringent regulators of medical radiation in the U.S., and errors are likely underreported to state regulators. In the more than two years since that article was published, there has been a substantial focus on safety in radiation therapy among lawmakers and radiation therapy-related professional societies. Congress held hearings on medical radiation safety in February 2010, and the American Society of Radiation Oncologists (ASTRO) issued a six-point plan to improve quality and safety for IMRT.

IMRT is administered using linear accelerators, which produce ionizing radiation for medical purposes. Linear accelerators are regulated by the Food and Drug Administration at the federal level and the Michigan Department of Community Health at the state level.

Registration of Radiation Therapy Facilities and Equipment

In Michigan, all facilities with linear accelerators – and each linear accelerator – must be registered with the Radiation Safety Section of the Michigan Department of Community Health (MDCH).[15] Registration comes with several conditions. Facilities must develop a written quality assurance plan of adequate scope to ensure that radiation is administered safely and effectively. They also must report misadministrations of medical radiation to the Radiation Safety Section.

Radiation facilities are inspected once when they first register and every four to five years after that. The purpose of the inspection is to take radiation shielding measurements, observe the quality assurance procedures set up by the facility, and check calibration records for the equipment. Calibration is required annually. Facilities that do not meet conditions of registration are given 30 days to take corrective action. Failure to take corrective action can result in either additional inspections and fees or civil fines, although in the experience of the MDCH regional physicist, these penalties are extremely rare. In Michigan, facilities are responsible for creating their own quality assurance plans. Some states, such as New York, recommend that quality assurance programs incorporate specific elements but allow individual facilities to develop their own protocols.[16]

Reporting of Radiation Therapy Misadministrations and Injuries

The open reporting of errors in radiation therapy can help practices learn from each other how to improve processes and increase patient safety.[17] Reporting of misadministrations of radiation therapy is required in Michigan for any error "resulting in a total radiation dose differing by more than +/- 10% of the total prescribed dose or errors resulting in a radiation dose greater than 25 percent of the prescribed dose for any treatment fraction."[18] Errors of this magnitude are not expected to result in adverse medical outcomes for the patient, but signal a failure within the system that must be remedied. Operators must report the error, corrective action taken, and any adverse events resulting from the misadministration.

Very few misadministrations have been reported. Between 2000 and 2010, 27 misadministrations were reported, or an average of 2.5 events per year.18 Three of these resulted in known adverse outcomes, 11 were not expected to result in any adverse outcomes, and 13 had an unknown effect. The reported number is likely to be a dramatic underreporting of actual errors. Studies of error rates in radiation therapy have generated estimates of 0.064 percent to 0.39 percent.[19,20,21] The reported error rate in Michigan is 0.00052 percent, or less than 1/100th of the most conservative estimated error rate.

Although underreporting to state regulatory bodies is somewhat expected, Michigan still has a far lower rate of error reporting than New York state, which has similar reporting rules but is considered a strict regulator. New York reports 16 times as many errors per 100,000 in population than are reported in Michigan (0.397 errors per 100,000 in New York, compared to 0.025 errors per 100,000 in Michigan).

Education and Training for Radiation Therapy Staff

Radiation therapy is administered by a team of professionals who are all responsible for different parts of the process and must work together to assure quality and safety. Radiation therapists administer the treatments, medical dosimetrists use software to create the treatment plan, and medical physicists perform quality assurance on hardware and software and ensure that the treatment plan is accurate. In some institutions, medical physicists are involved in treatment planning. Currently there is no required level of education or training for non-physicians who work planning or delivering radiation therapy in Michigan, nor are they required to be licensed by the state. Currently 33 states require radiation therapists to be licensed by a state accrediting board, with many relying on the American Registry of Radiologic Technologists (ARRT) to provide the certification necessary for licensure.[22] The Medical Dosimetrists Certification Board certifies dosimetrists and both the American Board of Radiology and the American Board of Medical Physics certify medical physicists. Individual facilities may require these certifications as a condition of employment, but they are not currently required by the state.

Since 1999, the American Society of Radiation Therapists has introduced federal legislation that requires basic education and certification requirements for health care workers who administer radiation therapy. The Consistency, Accuracy, Responsibility and Excellence in Medical Imaging and Radiation Therapy (CARE) bill would ensure that patients have assurance of the same level of quality as those undergoing mammograms do under the Mammography Quality Standards Act.

Licensing and Accreditation

Radiation therapy facilities must be registered, but they are not required to be licensed or accredited in Michigan. Several other states require state licensing, but there is no central source that keeps track of how many states require licensing and what the licensing requirements are in those states.

Accreditation by the American College of Radiology-American Society for Radiation Oncology Accreditation Program is one option that allows facilities to demonstrate that they meet high standards of care for radiation oncology. Among the requirements for accreditation are adequate staffing levels, adequate levels of education and training for staff, quality assurance/quality control documentation, and self-assessment data based on chart review of actual cases. In 2011, only nine percent of radiation oncology practices were accredited by ACR-ASTRO.[23] In Michigan, only three facilities out of 75 in the state are accredited, and three more facilities are awaiting review for accreditation. Accreditation is one option for facilities that want to demonstrate a commitment to providing high quality and safe patient care, and while it remains rare in practice today, may be more common in the next few years.

Quality Assurance Concerns in IMRT

Improvements in the process of care are considered to be essential for efforts to improve patient safety in radiation therapy.[24] Taking a systems approach to preventing errors and taking human factors into account when designing ways to deliver care and assure quality can result in improvements in patient safety.

The complexity of IMRT requires substantial quality assurance procedures to ensure the safe administration of medical radiation. Quality assurance in IMRT is the subject of substantial research, with much of the research focusing on the mathematical models and automated techniques used for assuring that IMRT software and equipment are delivering the proper plans and doses.

There is some evidence that the highly automated nature of IMRT quality assurance removes the potential for human error and reduces error rates. Margalit et al[21] examined error rates within their institution for IMRT and compared them with error rates for 2D and 3D radiation therapy techniques. Because of the quality assurance procedures and care, there were significantly fewer errors with IMRT compared with 2D/3D techniques (0.033 percent vs. 0.072 percent). They conclude that technological advancements in radiation therapy may improve patient safety when combined with practice-based quality improvement procedures.

Checklists

Checklists have been shown to reduce complication rates and mortality when used for surgical procedures. Haynes et al found that the implementation of a 19 item checklist was associated with a reduction in in-hospital mortality from 1.5 percent to 0.8 percent and a reduction in complications from 11 percent to 7 percent.[25] Another study of checklists from de Vries et al showed a reduction in in-hospital mortality from 1.5 percent to 0.8 percent and a reduction in the total number of complications per 100 patients from 27.3 to 16.7.[26] These results show that checklists are a powerful tool for improving patient outcomes. Checklists adapted to radiation therapy have the potential to improve patient safety and quality of care.

Universal Protocol

The Universal Protocol is a series of steps required by The Joint Commission in accredited facilities to prevent wrong-site, wrong-patient, and wrong-procedure surgeries and procedures. Radiation therapy is exempted from the Universal Protocol.

One study of the Universal Protocol found it had the potential to reduce wrong-site surgery by 67 percent.[27] Whether this reduction would be seen in radiation therapy errors is unclear, but it demonstrates the reduction in errors that can be achieved by following a set procedure to verify that all patient information is correct. A protocol that is specific to radiation therapy and applies to both hospitals and freestanding radiation oncology centers could potentially reduce errors in radiation therapy administration.

Time Outs

One part of the Universal Protocol that has been tested in radiation therapy is the use of a "time out" before each procedure. A time out is a pause that allows the staff to verify that everything is correct and that all staff agree on the specifics of the procedure to be performed. One study has verified that a time out procedure is effective in reducing radiation misadministration errors. Rassmussen and Chu[28] examined misadministration records from five different cancer centers that implemented time out procedures between 2000 and 2009. They calculated error rates from the period before and after the time out was implemented, and found that the after the time out was implemented, misadministration errors were reduced threefold. A recent report commissioned by the American Society for Radiation Oncologists focused on safety in IMRT recommended the use of a "forced time out" to reduce errors and improve safety in IMRT procedures.[29]

Summary

IMRT is a newer technology that introduces new potential for error into the delivery of radiation therapy. Misadministration of radiation therapy can result in morbidity and mortality. Ensuring that IMRT is delivered in a safe and effective way requires attention to the process of care and appropriate regulation. Michigan's regulatory structure gives facilities most of the responsibility for implementing and monitoring quality assurance for IMRT and other radiation therapy. Reported errors in Michigan are much lower than reported error rates in the literature and in other states.

Some of the approaches that have been shown to improve quality of IMRT in the facility setting include: time outs, checklists, and the universal protocol.

Conclusion

IMRT is a relatively new option for the treatment of breast, lung and some other types of cancer, but has been used for head and neck, and prostate cancers for many years. These new applications of the technology require caution and a review of the available evidence. While IMRT has benefits related to toxicity in breast and lung cancer and possibly survival in lung cancer, more prospective studies are needed to confirm IMRT's advantages and determine who can most benefit from IMRT. As the use of the technology expands, vigilance is needed in protecting patient safety. Regulatory structures must adapt to the new complex requirements of IMRT, and facilities must constantly focus on quality improvement and safety. With these measures in place and more evidence in hand, IMRT can be used to improve the care of cancer patients without subjecting them to unnecessary risks.

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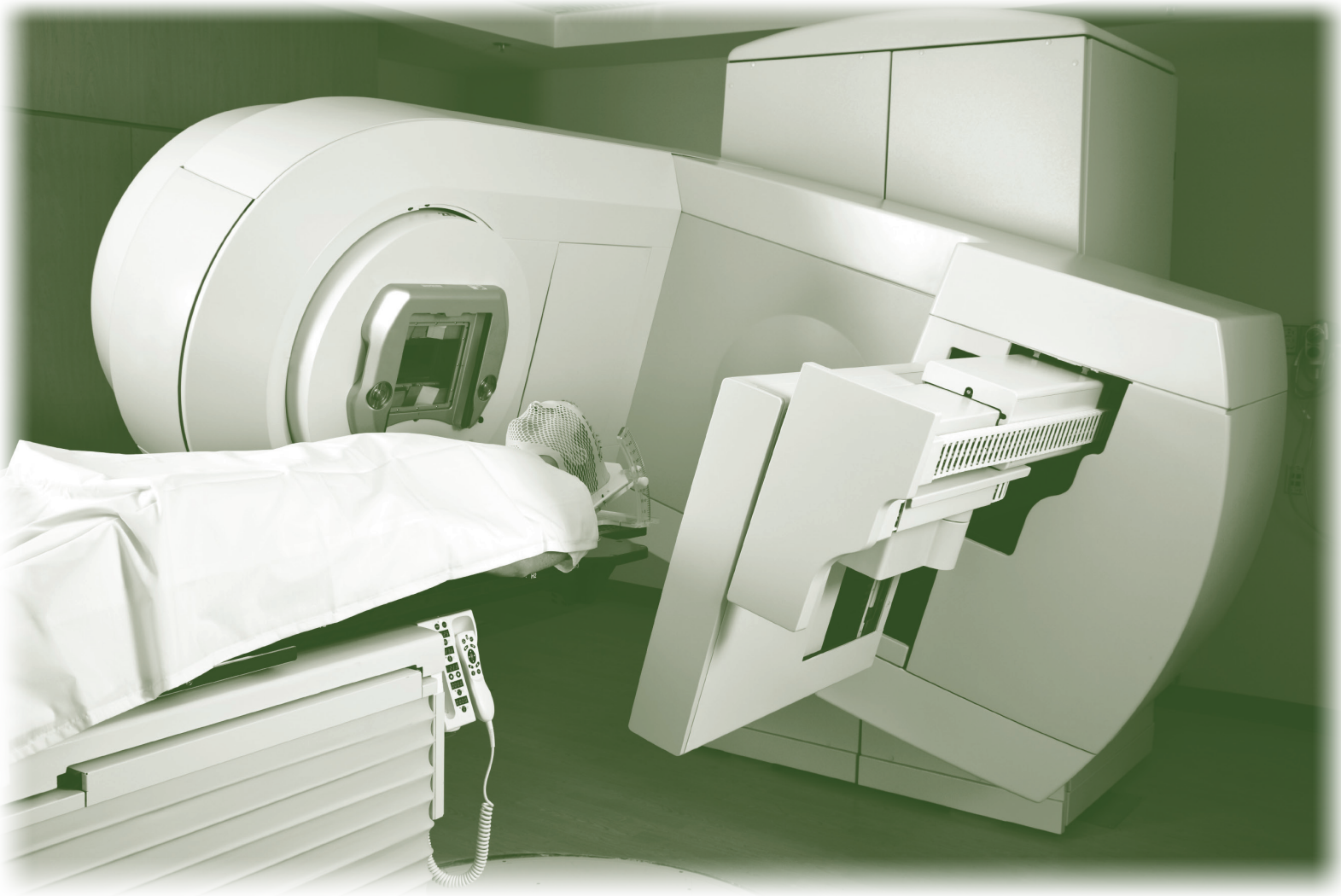

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