Intensity-Modulated Radiation Therapy Use in the U.S., 2004

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BACKGROUND. Intensity-modulated radiation therapy (IMRT) is a novel approach to the planning and delivery of radiation therapy. The prevalence of IMRT use among radiation oncologists in the U.S. appears to be increasing, despite limited data evaluating its risks and benefits.

METHODS. A random sample of radiation oncologists in the U.S., including a cohort of 441 physicians who were surveyed in 2002, was surveyed regarding IMRT use. IMRT users were questioned regarding their frequency of use, clinical applications, and reasons for adopting IMRT. IMRT nonusers were asked their reasons for not using IMRT, whether they planned to use it in the future, and reasons for wanting to adopt IMRT. Differences in responses between 2002 and 2004 were compared.

RESULTS. The survey was conducted between July 1, 2004 and August 31, 2004. Of 368 evaluable participants, 239 physicians (64.9%) responded. The proportion of respondents who used IMRT was 73.2% (175 physicians), compared with 32.0% in 2002. The adoption rate of IMRT among nonusers from 2002 to 2004 was 62.7% (95% confidence interval, 51.9–73.5%). Many IMRT users (81.0%) had used IMRT to deliver higher than conventional doses of radiation, predominantly in patients with genitourinary and head and neck tumors. Major reasons cited for IMRT adoption were permitting normal tissue sparing (88.0%), dose escalation (85.1%), and economic competition (62.4%). Ninety-one percent of nonusers planned to adopt IMRT in the future.

CONCLUSIONS. IMRT use among radiation oncologists in the U.S. has increased significantly since 2002. Standardized guidelines and careful, prospective analyses evaluating its risks and benefits are needed.

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KEYWORDS: intensity-modulated radiation therapy, physician education, standardized guidelines, survey.

Intensity-modulated radiation therapy (IMRT) is a novel approach to the planning and delivery of radiation therapy (RT). Unlike conventional RT, IMRT usually involves inverse planning, whereby dose-volume constraints for targets and normal tissues are defined a priori, then optimized with the use of a computer algorithm. Targets and normal tissues are first delineated on a computed tomography (CT) scan. The algorithm then identifies beam orientations and patterns of intensity that optimize conformality of the prescription dose to the shape of the target in three dimensions while sparing surrounding normal tissues. Treatment typically is delivered with the help of multileaf collimators, which consist of individual motorized leaves that can move in and out of the beam’s path during treatment, modulating the beam’s intensity.

Numerous investigators have demonstrated the benefits of IMRT planning in a variety of tumor sites in terms of the feasibility of...
normal tissue sparing\textsuperscript{2–7} and the delivery of higher than conventional doses.\textsuperscript{8,9} Preliminary reports involving treated patients also have been promising, with low rates of toxicity,\textsuperscript{10–19} even when higher than conventional doses are delivered.\textsuperscript{18,19} Tumor control rates have compared favorably with the rates reported in conventional RT studies,\textsuperscript{11,18–23} particularly in patients treated with escalated doses.\textsuperscript{18,19} IMRT also may provide a safer and more effective means of retreatment previously irradiated patients.\textsuperscript{24,25}

Despite such promise, IMRT is a time-intensive and labor-intensive process, and it requires considerable investments in both software and hardware. To our knowledge, few guidelines exist to date regarding how it should be performed outside of a protocol or investigative setting.\textsuperscript{26,27} The steep dose gradients inherent with IMRT may be troublesome in sites with considerable organ motion, such as the lung and upper abdomen.\textsuperscript{28} Although IMRT may be cost effective compared with conventional RT in select patients,\textsuperscript{29} it remains unclear whether it is cost effective generally, given its increased expense. Moreover, published outcome studies mostly are retrospective and have included limited numbers of patients with relatively short follow-up. Finally, an elevated risk of second malignancies in patients who receive IMRT also has been hypothesized.\textsuperscript{30}

Notwithstanding these concerns, interest in IMRT is increasing in the radiation oncology community. In 2002, we performed a nationwide practice survey and reported that 32% of practicing radiation oncologists were using IMRT in their clinics.\textsuperscript{31} However, the majority of respondents only recently had adopted IMRT, and nearly all nonusers stated their intention to begin using it in the near future. To update these results and to characterize further the use of IMRT in this country, we performed a follow-up survey. The results of this survey and the implications of our findings are presented herein.

**MATERIALS AND METHODS**

**Sample**

In 2002, a random sample of 450 radiation oncologists from the 2000 American Society of Therapeutic Radiology and Oncology (ASTRO) directory was selected. ASTRO is the largest association of radiation oncologists, with approximately 3800 active members. The current sample consisted of this same cohort, less nine physicians who had retired. An additional 59 physicians were selected randomly from the 2004 ASTRO directory, making a total sample size of 500. Only physicians designated as “active” were selected. Contact information for the 441 physicians who were surveyed in 2002 was updated using the 2004 directory. Between July 1, 2004 and August 31, 2004, surveys were sent by fax and, if available, by e-mail. If no fax number was listed, physicians were contacted by telephone to obtain their correct fax number. If no telephone contact could be established and no valid fax number was obtained, the physician was designated as “uncontactable.” Recipients who did not respond to the initial fax or e-mail were sent the survey a second time; if no response was received, then they were designated “nonrespondents.” Respondents and nonrespondents were considered “evaluable”; uncontactable physicians, retirees, and those who had relocated or were on leave or extended vacation were considered “nonevaluable.” The response rate was defined as the number of respondents divided by the number of evaluable physicians.

**Survey**

Survey questions were similar or identical to those from the prior survey.\textsuperscript{31} In brief, physicians were asked their gender, type of practice (academic or private), size of practice, year they began practicing, whether they were using IMRT, and their future plans regarding IMRT use. IMRT was defined specifically to involve the use of inverse planning.

IMRT users also were questioned regarding the number of patients and range of disease sites treated with IMRT, predominant site(s) treated, where they learned to use IMRT, and the proportion of their patients currently treated with IMRT. Users also were asked whether they had used IMRT to escalate dose, “dose paint” (i.e., deliver different doses to different parts of the target), reirradiate, or treat a patient with palliative intent. IMRT nonusers were asked their reasons for not using or ceasing to use IMRT, whether and when they planned to use it in the future, and, if they planned to adopt IMRT, their reasons for wanting to do so. Nonrespondents from the 2002 survey were asked to recollect whether they were using IMRT prior to July 2002 (the time of our previous survey) to ascertain whether there was evidence of nonresponse bias.

**Statistical Analysis**

The sample size of 500 represented approximately 13.2% of active ASTRO members. As in our prior survey, a subgroup analysis of academic versus private practitioners was planned. Based on the previous response rate of 51% and a proportion of 23% of responding physicians who were academics, we estimated that a sample size of 500 would be necessary to provide > 80% power to detect an absolute difference of 25% (for $\alpha = 0.05$) in proportions between these subgroups.
Differences in proportions between groups were compared with the chi-square test. Differences in means were compared with analysis of variance. A P value < 0.05 was considered statistically significant. When indicated in the text, responses were adjusted for unit nonresponse using a probability (adjustment cell) approach. For this adjustment, the probability of response conditional on IMRT use was estimated by using the prevalence of IMRT use among nonrespondents from the 2002 survey. A logistic model was used to predict growth of IMRT use. All statistical analyses were conducted using SAS software (SAS Institute, Inc., Cary, NC).

RESULTS

Of the 500 radiation oncologists selected, 132 were nonevaluable (50 uncontactable, 46 retired, 30 relocated, 6 on leave/vacation). Of the 368 evaluable physicians, 239 responded (response rate, 64.9%). Respondents included 114 individuals who responded to the 2002 survey, 93 nonrespondents from the 2002 survey, and 32 individuals from the new sample. Respondents represented 44 states and the District of Columbia.

Demographic characteristics of respondents are summarized in Table 1. Of the 239 respondents, 175 physicians stated that they use IMRT, for a prevalence of 73.2% (95% confidence interval [95% CI], 67.6–78.8%). Adjusting for nonresponse bias, the prevalence of IMRT use was 67.8% (95% CI, 61.1–74.5%). For comparison, the percentage of respondents using IMRT in 2002 was 32.0%.

IMRT users had a lower mean number of years in practice (15.2 yrs vs. 16.8 yrs; P < 0.029) and larger practice size (P < 0.001) than nonusers (Table 1). IMRT use did not appear to differ according to gender (P = 0.74) or region (P = 0.86). Academic physicians were more likely to use IMRT (80.7% vs. 70.9%) than private practitioners; however, this difference was not statistically significant (P = 0.14). For comparison, the corresponding percentages in 2002 were 51.2% and 26.4% for academic physicians and private practitioners, respectively (P = 0.003).

Most IMRT users began using IMRT after 2001 (Fig. 1). Of 75 respondents to the 2004 survey who were nonusers in 2002, 49 respondents (65.3%) were now using IMRT, for an adoption rate (adjusted for nonresponse bias) of 62.7% (95% CI, 51.9–73.5%) over 2 years. Based on these figures, an estimated 82.6% of radiation oncologists will be using IMRT by mid-2006 (95% CI, 77.9–86.5%).

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Among the 175 IMRT users, the most common reasons cited for adopting IMRT were to spare normal tissue/optimize conventional dose delivery (88.0%)
and escalate dose (85.1%) (Table 2). Other reasons included remaining competitive with other centers (49.1%), gaining a competitive advantage (29.5%), and, for the 46 academic IMRT users, performing clinical research (56.5%). Economic competition (gaining an advantage or remaining competitive) was cited as a reason for IMRT adoption by 62.4% of respondents and was cited more commonly as a reason by physicians in private practice than academia (67.2% vs. 48.9%; \( P = 0.029 \)).

The most common sites treated with IMRT were genitourinary, head and neck, and central nervous system tumors (Table 2). Private practitioners were more likely than academic physicians to have used IMRT to treat a patient with genitourinary carcinoma (93.0% vs. 60.9%; \( P < 0.01 \)), whereas academic physicians were more likely to have treated a pediatric patient with IMRT (30.4% vs. 0.6%). Although 42% of IMRT users had treated \( > 50 \) IMRT patients, the majority (73.0%) stated that they treated \( < 25 \)% of their current patients with IMRT. Academic physicians tended to treat a greater proportion of their patients with IMRT than private practitioners (\( P = 0.054 \)) (Table 2). The percentages of IMRT users who planned to increase, maintain, or decrease their current level of IMRT use were 62.8%, 35.8%, and 1.7%, respectively.

The majority of IMRT users (81.0%) had used IMRT to deliver higher than conventional doses, predominantly in patients with genitourinary malignancies and head and neck tumors. Less common sites treated with dose escalation included lung, gynecologic, central nervous system, and gastrointestinal tract tumors. Dose escalation was common equally among private practitioners and academic physicians. Dose painting, reirradiating, and palliating with IMRT were common in both groups, with academic physicians more likely to use IMRT to reirradiate or palliate (Table 2). IMRT users learned how to use IMRT from a variety of sources (Fig. 2).

Of the 64 IMRT nonusers, 11 respondents (17.2%) stated that they were in the process of implementing IMRT in their clinics. Forty-four respondents (68.8%) stated that they lacked the necessary equipment to treat patients with IMRT, and 11 respondents (17.2%) cited insufficient staffing as a primary reason they were not using IMRT. Fifty-eight respondents (90.6%) stated they planned to use IMRT in the future, with 38 respondents (59.4%) planning to adopt it within the next year.

**DISCUSSION**

IMRT use among radiation oncologists in the U.S. increased markedly between 2002 and 2004. Primary reasons for adopting IMRT have been the ability to spare normal tissue and escalate dose. Correspondingly, studies supporting the use of IMRT for these purposes are appearing in the literature. The rapid adoption of IMRT, however, also has been driven in part by economic incentives. Meanwhile, long-term data assessing risks of IMRT and prospective controlled trials establishing a benefit to IMRT over conventional therapy are to our knowledge lacking. Although most radiation oncologists currently use IMRT to treat a small percentage of patients, the number of patients treated with IMRT is likely to rise substantially in the near future. Patients and physicians should be aware of the important issues associated with the rapid emergence of this technology.

The advent of IMRT with inverse planning represents a significant advance in the ability to deliver conformal RT. The ability to create highly conformal dose distributions with photon beams (as opposed to less commonly used forms of conformal radiation, such as proton therapy) can lead to large reductions in the volume of normal tissue receiving high-dose radiation. Preliminary data suggest that normal tissue sparing with IMRT can reduce both acute and late toxicity without compromising tumor control. Dose-escalation studies have shown that IMRT can be used to safely deliver higher doses of radiation with correspondingly high rates of tumor control. By favorably altering the therapeutic ratio of RT, IMRT also enables the safe delivery of radiation to patients who have organ sensitivity that otherwise would limit or prohibit its use. These data suggest considerable promise for IMRT to benefit cancer patients.

Because toxic effects of combined-modality ther-
apy frequently are superimposed, IMRT also has significant potential to reduce toxicity and improve therapeutic efficacy of multimodality treatment regimens. For example, studies have shown that bone marrow sparing with IMRT is associated with less hematologic toxicity in patients undergoing whole pelvic irradiation.6,34 The association between bone marrow sparing with IMRT and improved ability to tolerate chemotherapy and a reduced need for antiemetic medication, colony-stimulating factors, and erythropoietic hormones is an ongoing area of investigation. Whether normal tissue sparing with IMRT can reduce morbidity associated with surgery in irradiated patients is another hypothesis to be explored.

Although a strong theoretic basis and many published studies have provided a rationale for IMRT use, the results of the current study demonstrate that a leading motivation to adopt IMRT, particularly in the private practice community, has been economic competition. In 2000, the Centers for Medicare and Medicaid Services increased reimbursement rates for IMRT to four times the rate for conventional therapy, which has provided a significant incentive for its adoption. These rates, however, recently have been

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of academics (%)</th>
<th>No. in private practice (%)</th>
<th>Total (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMRT users</td>
<td>46 (80.7)</td>
<td>129 (70.9)</td>
<td>175 (100.0)</td>
<td>0.14</td>
</tr>
<tr>
<td>Reasons for using/adopting IMRT*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spare normal tissue/optimize delivery of conventional doses</td>
<td>41 (91.1)</td>
<td>113 (88.3)</td>
<td>154 (88.0)</td>
<td>0.60</td>
</tr>
<tr>
<td>Escalate dose</td>
<td>33 (73.3)</td>
<td>116 (90.6)</td>
<td>149 (86.1)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Economic competition</td>
<td>22 (46.9)</td>
<td>86 (67.2)</td>
<td>108 (62.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Remain competitive</td>
<td>15 (33.3)</td>
<td>70 (54.7)</td>
<td>85 (49.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Gain a competitive advantage</td>
<td>12 (26.7)</td>
<td>39 (30.5)</td>
<td>51 (29.5)</td>
<td>0.63</td>
</tr>
<tr>
<td>Research</td>
<td>26 (57.8)</td>
<td>17 (13.3)</td>
<td>43 (24.5)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Other</td>
<td>2 (4.4)</td>
<td>4 (3.1)</td>
<td>6 (3.5)</td>
<td>0.68</td>
</tr>
<tr>
<td>Disease sites treated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>26 (60.9)</td>
<td>119 (93.0)</td>
<td>147 (84.5)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Head and neck</td>
<td>35 (76.1)</td>
<td>105 (82.0)</td>
<td>140 (80.5)</td>
<td>0.38</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>32 (70.0)</td>
<td>85 (66.4)</td>
<td>117 (67.2)</td>
<td>0.70</td>
</tr>
<tr>
<td>Gynecology</td>
<td>12 (26.1)</td>
<td>35 (27.3)</td>
<td>47 (27.0)</td>
<td>0.87</td>
</tr>
<tr>
<td>Breast</td>
<td>12 (26.1)</td>
<td>34 (26.6)</td>
<td>46 (26.4)</td>
<td>0.95</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>13 (28.3)</td>
<td>33 (25.8)</td>
<td>46 (26.4)</td>
<td>0.74</td>
</tr>
<tr>
<td>Lung</td>
<td>12 (26.1)</td>
<td>20 (15.6)</td>
<td>32 (18.4)</td>
<td>0.12</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>8 (17.4)</td>
<td>22 (17.2)</td>
<td>30 (17.2)</td>
<td>0.97</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>14 (30.4)</td>
<td>8 (6.5)</td>
<td>22 (12.6)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>5 (10.9)</td>
<td>16 (12.5)</td>
<td>21 (12.1)</td>
<td>0.77</td>
</tr>
<tr>
<td>Other</td>
<td>3 (6.5)</td>
<td>2 (1.6)</td>
<td>3 (1.7)</td>
<td>0.08</td>
</tr>
<tr>
<td>No. of patients treated</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 50</td>
<td>24 (52.2)</td>
<td>49 (38.3)</td>
<td>73 (42.0)</td>
<td>0.16</td>
</tr>
<tr>
<td>11–50</td>
<td>13 (28.3)</td>
<td>56 (43.8)</td>
<td>69 (39.7)</td>
<td>0.16</td>
</tr>
<tr>
<td>1–10</td>
<td>9 (19.6)</td>
<td>23 (18.0)</td>
<td>32 (18.4)</td>
<td>0.16</td>
</tr>
<tr>
<td>Percent of current patients treated with IMRT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 75%</td>
<td>2 (4.3)</td>
<td>0 (0.0)</td>
<td>2 (1.1)</td>
<td>0.050</td>
</tr>
<tr>
<td>51–75%</td>
<td>3 (6.5)</td>
<td>3 (2.3)</td>
<td>6 (3.4)</td>
<td>0.38</td>
</tr>
<tr>
<td>25–50%</td>
<td>9 (19.6)</td>
<td>30 (23.4)</td>
<td>39 (22.4)</td>
<td>0.16</td>
</tr>
<tr>
<td>&lt; 25%</td>
<td>32 (69.6)</td>
<td>95 (74.2)</td>
<td>127 (73.0)</td>
<td>0.16</td>
</tr>
<tr>
<td>Percent using IMRT to escalate dose</td>
<td>34 (73.9)</td>
<td>107 (83.8)</td>
<td>141 (81.0)</td>
<td>0.15</td>
</tr>
<tr>
<td>Percent using IMRT to reirradiate</td>
<td>36 (78.3)</td>
<td>76 (59.4)</td>
<td>112 (64.4)</td>
<td>0.020</td>
</tr>
<tr>
<td>Percent using IMRT to dose paint</td>
<td>27 (58.7)</td>
<td>75 (58.6)</td>
<td>102 (58.6)</td>
<td>0.099</td>
</tr>
<tr>
<td>Percent using IMRT to palliate</td>
<td>26 (56.5)</td>
<td>47 (36.7)</td>
<td>73 (40.7)</td>
<td>0.020</td>
</tr>
</tbody>
</table>

IMRT: intensity-modulated radiation therapy.

*Note that 1 physician in each category (academic, private practice) did not respond to these questions; thus, percentages are out of 45 and 128 respondents, respectively (totals are out of 173 respondents).
reduced to approximately triple the rate for conventional therapy.\textsuperscript{35} It is noteworthy that a greater percentage of respondents in the current survey, compared with the 2002 survey, cited the desire to \textit{remain} competitive (as opposed to \textit{gaining} a competitive advantage). Given the increasing prevalence of IMRT use in the radiation oncology community and increased attention in the media\textsuperscript{36} and on the Internet,\textsuperscript{37} physicians or centers that do not offer this technology may be feeling pressure to adopt it. False or misleading statements touting unproven benefits of IMRT have appeared on numerous websites, including some that belong to major academic centers.\textsuperscript{37} The cost-benefit ratio of IMRT also is unknown, although a recent study reported that it is cost-effective compared with three-dimensional conformal therapy in patients with intermediate-risk prostate carcinoma.\textsuperscript{29} The relation between economic incentives and increased IMRT utilization, therefore, raises important questions regarding ethical practices and appropriate resource allocation.

Given the technical complexities of IMRT planning and delivery, there is an increasing need for standardized guidelines both to provide methodology for controlled trials and to ensure quality control when IMRT is implemented outside of research settings. Many concerns about the safety and efficacy of IMRT still exist, including increased machine head leakage through multileaf collimators and the spread of low-dose radiation to normal tissue, potentially increasing the risk of second malignancies;\textsuperscript{30} decreased dose rate and increased dose heterogeneity within targets, with unclear radiobiologic consequences;\textsuperscript{38} and steep dose gradients around targets that can move during and between treatments, potentially compromising target coverage and tumor control.\textsuperscript{27}

Although general guidelines for IMRT use currently exist,\textsuperscript{39} and guidelines are now being set for its use in cooperative group trials, many specific (but fundamental) issues, such as how targets should be defined, how to account for organ motion, and what criteria should be used to judge the acceptability of a plan, to our knowledge have not been standardized for most disease sites. However, published guidelines for specific clinical situations are emerging.\textsuperscript{26,27} In addition, most residency programs now provide didactic and practical IMRT education for their residents.\textsuperscript{30} Seminars and practicums sponsored by professional societies, academic institutions, and vendors constitute another important source of hands-on IMRT training. Nonetheless, many specifics pertaining to how IMRT is being implemented in the community are unknown.

The current study had several limitations. The sample drawn from ASTRO members may not have been representative of the entire population of radiation oncologists and may have led to over-sampling of academic physicians. Approximately 35% of the evaluable sample did not respond, and 10% of the total sample was uncontactable, which could bias our results, although nonresponse bias appeared to affect our estimates only modestly. Aspects of IMRT use, such as the quality of plans or treatment, target delineation, treatment delivery, and quality assurance, were beyond the scope of the current survey. Our analysis was restricted to IMRT involving inverse planning; techniques using forward planning with multiple segments were not considered. Finally, some definitions were not defined strictly and therefore could be construed differently by individual respondents.

Research to date suggests that IMRT has great potential to augment cancer treatment. However, many questions remain about its safe and appropriate use. Standardized guidelines increasingly are necessary to ensure continued delivery of high-quality radiation therapy. Prospective controlled trials evaluating tumor control and treatment sequelae, with careful follow-up to monitor long-term risks and benefits, will be needed as more patients are treated with IMRT. To the extent that this change affects patients with cancer in general, individuals involved in the care of these patients should be aware of key issues regarding IMRT.

REFERENCES


