



Lucy Kettlewell. *Boats, Michigan #1*. Oil on board. From the personal collection of John Horton.

Advances in stereotactic radiation techniques have resulted in safer delivery of high doses to extracranial sites with reduced toxicity and improved outcomes.

Stereotactic Body Radiation Therapy: Transcending the Conventional to Improve Outcomes

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Background: Intracranial delivery of high-dose radiation treatment with stereotactic techniques has paved the way for treatment of extracranial sites.

Methods: The authors review the evolution of stereotactic body radiation therapy (SBRT) and its application to tumors in the lung and abdomen, addressing both the technical concerns associated with treatment delivery and the emerging clinical data.

Results: Radiation delivery systems have overcome the obstacles with immobilization, respiration, visualization, and daily reproducible imaging. Lung SBRT has been associated with local control rates of over 90%, and liver SBRT has ranged from 55% to 93%. SBRT is being explored in other sites such as the pancreas and kidney. Mature data from ongoing trials will be available in the next 5 years.

Conclusions: Modern stereotactic radiation treatment techniques allow the safe delivery of high doses to extracranial sites with minimal toxicity, which results in improved outcomes.

Introduction

Improvements in radiological imaging and increasingly sophisticated treatment planning and delivery systems have revolutionized the field of radiation oncology. Modern techniques permit radiation oncologists to escalate radiation dose to tumors while simultaneously minimizing dose to normal tissues in ways previously

not possible. Stereotactic body radiation therapy (SBRT), defined as the treatment of an extracranial lesion with a single or very few (5 or fewer) high-dose fractions, is one such application of these technologies. While this technique has been utilized for intracranial lesions for many years, it has only recently been used for extracranial disease. This review explores the emergence of SBRT as a new treatment modality for lung and abdominal tumors.

Intracranial Origins

In the late 1940s, Leksell¹ developed a stereotactic apparatus for human neurosurgery that consisted of a type of halo, designed to screw into the table of the patient's skull. The stereotactic device could then be attached to a table, thereby rigidly fixing the patient's

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Abbreviations used in this paper: SBRT = stereotactic body radiation therapy, RILD = radiation-induced liver disease.

brain lesion in 3-dimensional space. It used a polar coordinate system for localizing lesions. With this advance, radiation oncologists could treat small, isolated brain tumors more precisely. By targeting the lesion with tight margins and utilizing a large number of different angles for treatment, only a small number of beams traversed any given portion of brain. The result was that very high doses of radiation could be maximized to the target tumor while simultaneously minimizing damage to normal brain tissue. The technique was fairly refined by the early 1970s² and has been widely adopted since then.

Leksell's Gamma Knife system employs 201 Cobalt-60 sources (half-life: 5.26 years). The sources lie in a circular array within a shielded housing, with individual apertures that open when the patient is in the treatment position. The selection of the appropriate sources and individual exposure times for each source are derived using a computerized treatment planning system. The system has undergone numerous refinements.³ A relative disadvantage is that the radioactive sources lie within a dome with a relatively small opening, which is optimal for treating brain lesions but not other areas in the body. Furthermore, the sources must be replaced after several years due to radioactive decay. Subsequently, other manufacturers designed stereotactic radiotherapy systems for use with standard radiation linear accelerators. Typically, these involve some sort of specialized immobilization system that attaches to the linear accelerator treatment couch, thereby increasing versatility. Regardless of whether the treatment is delivered on a Gamma Knife unit or a standard linear accelerator, the end result is that the radiation is delivered to the desired target with an accuracy of a few millimeters.

Extracranial Evolution

While it is possible to screw a rigid frame into position against the skull, this type of immobilization solution has limited applicability in extracranial body sites. Consequently, a barrier to implementation of body stereotactic radiotherapy has been the development of suitably rigid immobilization systems with accurate patient positioning and reproducibility. Over the past 10 to 15 years, researchers have developed a number of solutions to these problems. As a result, radiation oncologists are now able to treat patients with extracranial disease with stereotactic techniques.

To do this, multiple technical issues must be accounted for and require the close collaboration of a multidisciplinary team that includes the radiation oncologist, medical physicist, radiation therapist, pulmonologist, gastroenterologist, and interventional radiologist. First, the area to be treated must be able to be reproducibly imaged on a daily basis. This may involve the implantation of markers into the region of interest. Termed *fiducials*, these markers are simple radio-

opaque spheres, coils, or seeds that are implanted in or near the tumor percutaneously, bronchoscopically, or endoscopically (Fig 1A-B). Second, the patient must undergo a CT simulation so that these markers and their relation to the tumor can be delineated. At simulation, the patient must be immobilized such that the treatment can be duplicated on a daily basis in a highly accurate way. At our institute, we use the BodyFIX System (Medical Intelligence, Munich, Germany). It incorporates a custom-made cradle that conforms to the patient and is attached to the treatment table. Third, a plastic cover sheet is then placed on the patient and taped down onto three sides of the cradle. Vacuum suction is applied to adhere the cover sheet tightly to the patient and cradle. The currently available immobilization systems position the patient with minimal daily setup variability — typically 4 mm or less.^{4,5} Fourth, the CT data must be transferred to the computer workstation so that the best treatment plan for the individual patient can be

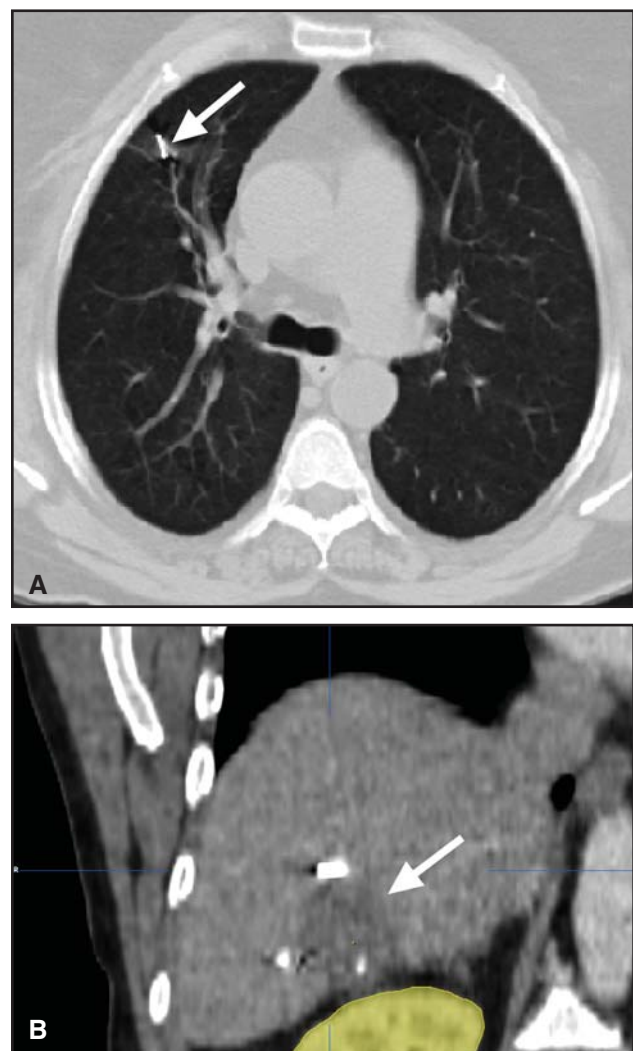


Fig 1A-B. — (A) One of several gold Visicoils implanted into a lung cancer patient, seen on CT scan taken 6 weeks after treatment (arrow). (B) Gold Visicoils implanted into the liver, seen in a coronal reconstruction of a CT scan. Note the hypodense liver lesion (arrow).

designed using software that displays in 3-D the tumor and normal tissues. Fifth, the treatment plan must account for the degree of motion with respiration.

Nearly all thoracoabdominal structures move during normal respiration. This poses a significant problem for the radiation oncologist. The larger the respiratory motion, the greater the amount of normal tissue that receives irradiation during the stereotactic treatment. Because of the high doses of radiation involved, normal tissue toxicity is a concern. One of the simpler techniques available to minimize diaphragmatic motion is the use of abdominal compression. A few such systems are commercially available. Typically, they involve use of a plate on the abdomen, onto which downward force is applied. This pressure reduces the amplitude of tumor motion by shifting the mode of inspiration away from reliance on diaphragmatic excursion and toward intracostal space expansion. If necessary, oxygen is supplied via nasal cannula for patient comfort.

Radiation oncologists account for the remaining tumor motion during the treatment planning process. The simplest way is to apply a standard margin around the tumor seen on the CT scan. However, this approach leads to increased radiation dose to normal tissues. A more sophisticated means is to perform a series of CT scans at different phases of the respiratory cycle. Newer CT simulators include such a “4-D” feature. The radiation oncologist then contours the tumor at different phases of the respiratory cycle. The resultant volumes are fused together and designated as the volume of interest for treatment. If the treatment center does not have a 4-D CT scanner, the radiation oncologist can perform multiple CT scans, with the patient breathholding at maximal inspiration and expiration.

If the tumor does not move significantly after all the planning has been completed, then the treatment can be delivered with normal respiration. If motion is still an issue, then the patient can be instructed in breathholding techniques. Another option that some centers have been using is to “gate” the treatment to the respiratory cycle so that the patient breathes normally

but the treatment beam automatically turns on/off at the appropriate time during normal respiration.

Treatment planning for the stereotactic setting differs markedly from the conventional setting. In conventional radiation treatment, small doses per fraction are delivered over a period of many weeks. With stereotactic treatment delivery, high doses are given over a few days. This mandates that an extensive process be followed to assure that the setup position is verified before the beam is turned on.

On each treatment day, once the patient is immobilized, CT or orthogonal x-ray images are taken to assess tumor motion. Slight shifts are applied to the treatment couch to place the tumor precisely within 3-D space at the location indicated on the treatment planning CT scan. These images are overlaid onto each other for verification. Various software packages are available that can then determine necessary shifts in the treatment couch position in order to place the tumor in the requisite location in 3-D space, prior to initiation of treatment. The result is that before each high-dose fraction of radiation, the position of the intended treatment is verified.

Lung

Surgery remains the standard of care for treatment of early-stage, peripheral non-small cell lung cancers. However, many patients are not candidates for resection due to poor baseline pulmonary function or other comorbidities. Over the past decade, a large number of institutions have gained experience in treating peripheral lung lesions with stereotactic radiotherapy. Because of concerns about toxicity to structures within the mediastinum, treatment of central lesions has not been routinely performed. A variety of radiation fractionation schema have been attempted in the treatment of T1-2 N0 lung tumors. Some of the trials and their reported results are listed in the Table.⁶⁻¹³

Most of these studies demonstrate a dose-response, with improved local control at radiobiologically higher doses.⁷ In the United States, some centers have advo-

Table. — Selected Reported Results in the Use of Stereotactic Radiotherapy for Treatment of Peripheral Lung Cancers

Authors	Sample Size	Total Dose/# of Fractions (fx)	Local Control	Follow-up (mos)	≥ Grade 3 Toxicity
Uematsu et al ⁶	50	50–60 Gy/5–10 fx	94%	60	0.0%
Onishi et al ⁷	251	18–75 Gy/1–22 fx	86%	38	5.4%
Nagata et al ⁸	45	48 Gy/4 fx	98%	30	0.0%
Timmerman et al ⁹	37	60–66 Gy/3 fx	95%	24	5.4%
Baumann et al ¹⁰	138	30–48 Gy/2–4 fx	88%	33	10.1%*
Zimmermann et al ¹¹	68	37.5 Gy/3 fx	88%	36	3.0%
McGarry et al ¹²	47	54–72 Gy/3 fx	87%	15	–
Xia et al ¹³	43	50 Gy/10 fx	95%	36	2.3%

*Some of the treated lesions were central in location, not peripheral, although the report does not clarify whether a central tumor location led to increased risk of treatment toxicity.

cated the fractionation scheme implemented by Timmerman et al⁹ (20 Gy to 22 Gy \times 3 fractions). However, in Japan, where results from a variety of fractionation schema have been reported, 12 Gy \times 4 fractions or 10 Gy \times 5 is typically utilized.⁷ It is not merely the prescribed dose that differs in these various protocols; other technical factors also vary, affecting the dose actually delivered to the tumor. Some protocols did not utilize heterogeneity corrections to calculate dose. Some studies specified the dose to the tumor isocenter, while others prescribed the dose to the tumor periphery. Furthermore, tumor motion was variably accounted for. Despite these differences, these fractionation schemas have led to uniformly high rates of local control, typically around 90% to 95%. Radiological evidence of tumor regression is often evident after only 6 weeks (Fig 2A-B).

Classically, it has been thought that higher dose per fraction of radiation translates into more damage to normal tissue. However, researchers have reported few



Fig 2A-B. — (A) Lung tumor, prior to stereotactic radiotherapy. (B) Lung tumor 6 weeks after stereotactic radiotherapy. Note the small area of residual linear scarring.

examples of toxicity greater than grade 2 that are attributable to the stereotactic treatment. Pneumonitis and rib fracture are the most commonly reported significant adverse events. However, even these events are relatively rare (Table). It will be important to follow these patients longer to ascertain whether these increased radiation doses translate into additional adverse events over time. Currently, the preponderance of data suggests that this is a safe and highly effective form of treatment for patients with few treatment alternatives.

Going forward, it will be necessary to acquire additional data via multi-institutional, randomized protocols. To that end, some large trials are completed, underway, or in the planning stages. Some goals are (1) to build on the results of a large, national multi-institutional trial of stereotactic radiotherapy utilizing the dosing scheme of 20 Gy \times 3 fractions (RTOG-0236, enrollment now completed, clinical follow-up ongoing, analysis planned in 2008), (2) to define the role of SBRT in patients who are operable candidates (RTOG-0618, underway in 2008), (3) to define the role of SBRT in patients with central lesions in a phase I dose escalation trial (RTOG-0633), and (4) to define the role of SBRT in patients with metastases to the lung (planned as a future RTOG protocol).

Liver

Liver-only metastasis continues to be a multidisciplinary management dilemma. There are subsets of patients who appear to have the potential to be cured if, indeed, they have a finite small number of metastases, a state that has been called *oligometastases*.¹⁴ Determining how to best achieve long-term survival for this group of patients is becoming an expanding clinical issue as more treatment choices become available.

Surgical resection has been the mainstay of treatment for the last few decades. Colorectal cancer patients have formed the largest group of patients with hepatic metastatic disease. For selected colorectal patients with resectable liver-only disease, 5-year survival rates have consistently been in the range of 30%.¹⁵ Fong et al¹⁶ reported on over 1,000 patients from Memorial Sloan-Kettering Cancer Center with a 5-year survival rate of 37% and a 10-year survival rate of 22%. In the multivariate analysis, increased risk for recurrent disease was seen for those patients with positive margins, extrahepatic disease, a node-positive primary, a disease-free interval from primary to metastases of less than 12 months, more than one hepatic tumor, the largest tumor $>$ 5 cm, and a carcinoembryonic antigen (CEA) level above 200 ng/mL.

Some institutions have reported even further improvements. Choti et al¹⁷ reported that the 5-year survival rate for those treated at Johns Hopkins Hospital was 58% from 1993 to 1999 compared with 31% from 1984 to 1992. In their analysis of their single institu-

tional data over 16 years, factors that were associated with an improved survival were number of tumors (≤ 3), negative margins, and a CEA of <100 . Investigators at M. D. Anderson Cancer Center¹⁸ recently reported that their institutional survival rate following hepatic resection of a solitary metastasis from a colorectal primary exceeds 70% at 5 years. Data from Duke University Medical Center have shown that there can be long-term survivors of breast cancer with hepatic-only disease as well, with a reported 22% long-term survival rate.¹⁹

Although hepatic resection remains the gold standard because of its improved outcomes, the rise of radiofrequency ablation, embolization, chemoembolization, and radioembolization has been providing additional options. These alternatives have been used primarily when the patient has unresectable disease, when resection would leave an inadequate liver remnant, or when the patient's medical status contraindicates surgery.

The optimal selection of treatment modality has become even more important now that solid tumor systemic therapies continue to improve and control extrahepatic disease. With the retrospective data touting the superiority of surgical resection, the question bearing more scrutiny is: What is the best nonsurgical alternative? This has led to a resurgence of interest in external-beam radiation now that treatment techniques have improved.

Historically, external-beam radiation has been explored for its palliative benefit in the context of whole-liver radiation. In the 1980s, the RTOG conducted a trial randomizing patients to whole-liver radiation alone or in combination with the radiosensitizer misnomidazole.²⁰ The dose used was 21 Gy to the whole

liver in 7 fractions. Pain relief was reported in 80% of the patients, with complete relief in 54%. The benefit was noted a median of 1.7 weeks after initiation of treatment and was associated with a median duration of 13.0 weeks. There was no significant treatment-related morbidity, and median survival was reported to be 4.2 months. Following the initial work with whole-liver radiation alone, Mohiuddin et al²¹ demonstrated that a boost dose of radiation in addition to whole-liver radiation was associated with an improved median survival. In this series of patients with metastatic colorectal cancer, the median survival associated with those patients receiving whole-liver irradiation alone was 4 months compared with 14 months in those patients who received a boost to the site of liver disease.

In the 1990s, investigators from the University of Michigan expanded this work with hepatic dose escalation.²² Their trials showed the benefit of escalating dose with conformal techniques while respecting the tolerance of the liver (Fig 3). Data from their phase I/II trial reported in 1995 showed an objective response in 50% of their patients and propelled them to further explore the role of higher-dose delivery. They demonstrated the importance of monitoring for radiation-induced liver disease (RILD) as well as strategies to prevent this complication.^{23,24} RILD is a clinical syndrome characterized by anicteric hepatomegaly, ascites, and elevated liver enzymes. The syndrome occurs typically 2 weeks to 4 months after completion of radiation treatment to the liver. At the microscopic level, there is evidence of venous congestion in the central portion on each lobule with sparing of the larger veins. If RILD occurs, the syndrome can progress in severe cases to liver failure and death.

Based on the improvements seen with dose escalation while respecting the tolerance of the liver, many centers have been exploring the role of stereotactic body radiation techniques. SBRT would allow higher radiobiological doses, less irradiation of adjacent normal tissues, and shorter overall treatment time. In 1994, investigators from the Karolinska Hospital in Sweden reported on a method for stereotactic high-dose radiotherapy for abdominal tumors.²⁵ They developed an extracranial stereotactic frame and used abdominal compression to reduce the movement of the diaphragm to 5 mm to 10 mm. For 90% of their patient setups, they found a reproducibility rate of 5 mm to 8 mm. Blomgren et al²⁶ were the first to subsequently publish clinical data using this approach to treat liver malignancies. They prescribed a dose to the planning target volume of 7.7 Gy to 30 Gy for 1 to 4 fractions. The central part of the tumor received about 50% higher dose than that of the periphery of the planning target volume by a planned inhomogeneous dose distribution. At a follow-up period of 1.5 to 38 months, the local rate of no progressive disease was 80%.

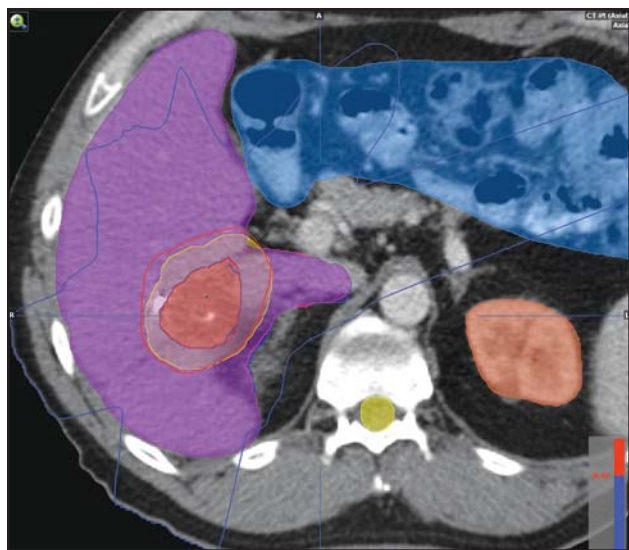


Fig 3. — Dose distribution in a highly conformal radiation treatment plan. The red and yellow shaded areas define the tumor to be treated. The surrounding red line represents the area receiving 100% of the prescribed dose. To achieve this conformality, a low dose of radiation is delivered to surrounding normal tissues (blue lines).

In 1997, German researchers began a trial exploring stereotactic single-dose radiation therapy of liver tumors. Herfarth et al²⁷ reported the results of their phase I/II trial that included 60 liver tumors in 37 patients. The dose was escalated from 14 to 26 Gy, with the 80% isodose surrounding the planning target volume. The median tumor size was 10 cm³. Results showed that the treatment was well tolerated with no major side effects. The overall actuarial local tumor control rates were 75%, 71%, and 67% at 6, 12, and 18 months of follow-up, respectively. If the first treated patients were grouped separately than the subsequent patients, the actuarial local control rate was 81% at 18 months. In the later-treated patients, stratification by size was not associated with a difference in local control rate of larger targets (≥ 15 cm³) vs smaller targets (<15 cm³). Lieskovsky et al²⁸ also reported data with single fractions of 18 and 22 Gy. In their phase I study, they have not yet reached the maximum tolerated dose at 22 Gy and are increasing the dose to 30 Gy.

The data reported so far with longer follow-up are encouraging. In a phase I study of SBRT for liver metastases, Schefter et al²⁹ showed the feasibility of delivering a dose of 60 Gy in 3 fractions to patients with one to three liver metastases. Last year, the data were updated from the continuation of that study as a phase II trial.³⁰ For the 28 discrete lesions treated with a median gross tumor volume of 14 cm³, the 18-month actuarial control estimate is 93%. There was no grade 4 toxicity. The patients included in their study either declined surgery or were considered to be technically or medically inoperable.

Other groups have focused on integrating a more protracted approach with 6 to 10 treatment fractions. Investigators from the University of Rochester Medical Center noted a median overall survival time of 14.5 months for their liver SBRT patients.³¹ They reported data on 69 patients with 174 treated metastatic liver lesions. The preferred treatment schedule in their study was 50 Gy in 5 Gy fractions over 2 weeks. The actuarial in field control rate of the irradiated lesions was 76% at 10 months and 57% at 20 months. The progression-free survival rate was 46% at 6 months and 24% at 12 months. No patients developed grade 3 or higher toxicity. Princess Margaret Hospital data reported by Dawson et al³² also reflects a hypofractionated approach. In their phase I/II trial, the investigators always delivered the stereotactic treatment in 6 fractions but individualized the prescription dose to maintain the same estimated risk of RILD based on a normal tissue complication probability (NTCP) model. The median prescribed dose was 36.6 Gy in 6 fractions. The Radiation Therapy Oncology Group is currently conducting an ongoing trial (RTOG-0438) to identify the maximally tolerated dose, up to 50 Gy in 5 Gy per fraction.

External-beam radiation has shown promise not only in the setting of metastatic lesions but also in primary hepatocellular carcinoma (HCC), a disease in which options are otherwise limited. Few medically fit patients present with early-stage disease. Those who do (with either a single nodule <2 cm to 5 cm or up to 3 nodules <3 cm) are considered for resection, liver transplantation, or percutaneous ablation.³³ In the last few decades, work has been done with conformal partial liver techniques. Seong et al³⁴ reported on patients with unresectable disease with a mean tumor size of 9.0 cm and with liver cirrhosis present in 90% of cases. The total dose received was adjusted by the volume of normal liver receiving radiation with a mean dose of 48.2 Gy in daily 1.8 Gy fractions. The response rate was 67% with a 2-year survival rate of 20% after radiotherapy and a 5% survival rate after 5 years. Dose was shown to be the only significant prognostic factor in multivariate analysis. Mornex et al³⁵ reported results from a French phase II trial of patients with one nodule <5 cm or up to two nodules <3 cm. They treated patients at 66 Gy at 2 Gy per fraction and found a complete response in 80%, a partial response in 12%, and stable disease in 8%.

Studies of SBRT for primary liver cancers are ongoing.^{32,36} Choi et al³⁷ reported their experience with 20 HCC patients treated with 50 Gy in 5 to 10 fractions with a tumor size of 2 cm to 6.5 cm. The overall response rate was 80%, with 20% complete responses. The disease-free survival rate was 65% at 1 year and 32.5% at 2 years. Tse et al³⁸ recently reported the Princess Margaret Hospital experience using the 6 fraction individualized dose approach described above to treat HCC and intrahepatic cholangiocarcinoma (IHC). Forty-one patients with unresectable Child-Pugh A HCC or IHC were included in the report. Median tumor size was 173 mL, and the median delivered dose was 36.0 Gy. No RILD or treatment-related grade 4/5 toxicity was seen within 3 months after treatment. Median survival of HCC and IHC patients was 11.7 months and 15.0 months, respectively.

Other Abdominal Sites

Stereotactic techniques are being applied to multiple other abdominal tumor sites. In pancreatic cancer, there is particular interest in exploring SBRT as a strategy of dose escalation. The majority (80% to 85%) of patients with this disease are diagnosed when their primary tumor is not operable. Data from the 1980s Gastrointestinal Tumor Study Group trial showed the importance of chemotherapy in conjunction with external-beam radiation with improved median survivals in the 10-month range compared with 5.7 months in the radiation-alone arm.³⁹ Further work with intraoperative radiation therapy and brachytherapy have shown improved outcomes with local control, but

not in survival and at the expense of increased toxicity from irradiation of adjacent organs.^{40,41} With the advent of better systemic chemotherapy regimens and SBRT, the issue for the future is determining the true benefit of a dose-intense, short-duration local modality. By accounting for respiratory motion and only targeting the gross target volume for stereotactic treatment, will we be able to demonstrate improved outcomes?

The results so far are mixed. Investigators from Aarhus University Hospital in Denmark explored stereotactic radiotherapy for patients with locally advanced, unresectable pancreatic cancer. In 2005, Hoyer et al⁴² reported the results of a phase II study of 22 patients who received a central dose of 15 Gy × 3 within 5 to 10 days. Only 2 patients (9%) were reported to have had a partial response; the remaining patients had either no change or disease progression. Median survival time was 5.7 months, and only 5% were alive at 1 year. Toxicity was significant, with 4 patients developing severe mucositis or ulceration of the stomach or duodenum, and 1 developing a nonfatal ulcer perforation of the stomach. Their group concluded that the treatment was associated with a poor outcome with unacceptable toxicity and was not recommended for advanced pancreatic cancer.

Data from Stanford University, however, have shown promise. Koong et al⁴³ reported the results of their phase I study of stereotactic radiosurgery in patients with locally advanced pancreatic cancer. All patients on the trial had 3 to 5 gold fiducials implanted into the tumor and then were treated with doses that were escalated from 15 to 25 Gy. Patients were selected if their tumor was <7.5 cm and had an Eastern Cooperative Oncology Group (ECOG) performance status of ≤2. Radiosurgery was done with the Cyberknife system (Accuray, Sunnyvale, California) in a single fraction to the gross pancreatic tumor only, excluding elective regional nodes. The investigators limited the dose to the small bowel since that was believed to be the most radiosensitive structure; the treatment plan was thus designed such that the 50% isodose line covered only the duodenal wall closest to the tumor. There was no significant gastrointestinal acute toxicity observed in the first 3 months. In the group treated to 25 Gy, the median overall survival was 8 months. All of these patients had local control of their tumors until death or last follow-up. The investigators concluded that a dose of 25 Gy would be recommended to achieve local control without significant toxicity.

A year later Koong et al⁴⁴ reported on 19 patients enrolled on a phase II trial that combined the 25 Gy radiosurgical boost with 45 Gy delivered in conventional fractionation with IMRT along with systemic 5-fluorouracil. In this study, patients were treated first with IMRT to the tumor and regional nodes concurrently with chemotherapy, which was delivered either

in the form of protracted venous infusion or as capecitabine. The 25 Gy radiosurgical boost was delivered within 1 month of completion as a boost to the gross tumor volume. The phase II trial was associated with more acute gastrointestinal toxicity than the phase I trial, with patients developing gastroparesis and duodenal ulcers. The local control rate was 94%, but systemic metastases progressed rapidly. Median overall survival was 33 weeks, with the site of first progression in all cases being distant.

The Karolinska Institute in Sweden⁴⁵ has been piloting the use of SBRT in the setting of primary and metastatic renal cell carcinoma. In a prospective phase II trial reported last year, 30 patients with inoperable renal cell carcinoma or metastatic disease received 2 to 4 fractions of SBRT with an overall survival of 32 months, a high degree of local control, and low toxicity.

Conclusions

High conformality with less normal tissue injury has been associated with improved control rates in the brain, so future research in extracranial sites holds substantial promise. By controlling the volume of normal tissues that receive high radiation dose with better targeting and real-time tracking systems, the path toward improved outcomes is becoming clearer. Can we cure a solitary primary or metastatic lung/liver tumor with SBRT? Can we combine better systemic chemotherapy with better radiation and cure pancreatic tumors? By transcending the conventional, we have now moved farther down that elusive road.

Disclosures

No significant relationship exists between the authors and the companies/organizations whose products or services may be referenced in this article.

The editor of Cancer Control, John Horton, MB, CbB, FACP, has nothing to disclose.

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