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A novel ytterbium-169 brachytherapy source and delivery system for use in conjunction with minimally invasive wedge resection of early-stage lung cancer

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Abstract

PURPOSE—To describe a novel source–delivery system for intraoperative brachytherapy in patients with early-stage lung cancer that is readily adaptable to a video-assisted thoracoscopic surgery approach and can be precisely delivered to achieve optimal dose distribution.

METHODS AND MATERIALS—Radioactive ytterbium-169 (¹⁶⁹Yb) was sealed within a titanium tube 0.28 mm in diameter and then capped and resealed by titanium wires laser welded to the tube to serve as the legs of a tissue-fastening system. Dose simulations were performed using Monte Carlo computer code (Los Alamos National Laboratory, Los Alamos, NM) to mimic the geometric and elemental compositions of the source, fastening apparatus, and surroundings.

RESULTS—Five test source capsules were subjected to a tensile load to failure. Failure in each capsule occurred in the wire of the fastener leg; there were no weld failures. Monte Carlo simulations and subsequent dose measurement showed the perturbation by the source legs in the deployed (bent over) position to be small (4–5%) for ¹⁶⁹Yb and much less than that for iodine-125 (32%).

CONCLUSION—We have developed a ¹⁶⁹Yb brachytherapy source–delivery system that can be used in conjunction with commercially available surgical stapling instruments, facilitates the precise placement of brachytherapy sources relative to the surgical margin, assures the seeds remain fixed in their precise position for the duration of the treatment, overcomes the technical difficulties of manipulating the seeds through the narrow surgical incision associated with video-assisted thoracoscopic surgery, and reduces the radiation dose to the clinicians.

Keywords

Radiation; Brachytherapy; Lung cancer; VATS; Wedge resection

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Introduction

For Stage I non-small-cell lung cancer, surgical resection is the definitive treatment, and lobectomy is the procedure of choice (1–3). Patients with poor pulmonary function or other significant medical comorbidities are generally considered to be poor candidates for lobectomy and have traditionally undergone limited resection in an attempt at lung preservation while achieving adequate surgical margins. In such patients, sublobar resection alone is associated with a three-fold increase in disease recurrence and 50% decrease in survival (4, 5). The addition of intraoperative brachytherapy using permanent interstitial implants has improved local control in patients undergoing wedge resection for Stage I lung cancers (6–9). For patients undergoing sublobar resection with brachytherapy, overall survival is comparable to that in patients undergoing lobectomy (9).

In clinical practice and, most recently, in the American College of Surgeons Oncology Group Z4302, a multi-institutional randomized prospective trial evaluating radioactive seed placement in patients with lung cancer medically unfit for lobar resection (10), iodine-125 (^{125}I) seeds are used as the permanent brachytherapy source (6–10). Ytterbium-169 (^{169}Yb) has been investigated as an alternative to ^{125}I for permanent interstitial implants with a higher photon energy of 92.7 keV, a shorter half-life of 32 days, a higher initial dose rate, and improvements in dose homogeneity (11–13).

Among the limitations inherent in all of the currently applied techniques are the inability to allow for adaptable and dynamic treatment planning in the operating room, the difficulty in precisely delivering the brachytherapy seeds intraoperatively to achieve the proper dose distribution after reinflation of the lung, and unnecessary radiation exposure to operating-room personnel (14). Furthermore, many of the current brachytherapy approaches are not readily adaptable to contemporary minimally invasive surgical techniques, including video-assisted thoracoscopic surgery (VATS).

We describe in this report the development of a ^{169}Yb brachytherapy source-delivery system that will facilitate the precise placement of brachytherapy sources relative to the surgical margin, assure the seeds remain fixed in their precise position for the duration of the treatment, overcome the technical difficulties of manipulating the seeds through the narrow surgical incision inherent in minimally invasive procedures, and reduce the radiation dose to the clinicians. We also report the dosimetric advantages of the ^{169}Yb source staple.

Methods and materials

Design criteria

A source and delivery system was designed to be used in conjunction with commercially available surgical stapling instruments widely used for VATS. By integrating a permanent brachytherapy source into the mature technology of a surgical stapling device, we aimed to use a single instrument to cut and seal lung tissue and simultaneously place a permanent radioactive seed implant. As such, the following design criteria were established: (1) The source/staple must not compromise the preestablished parameters of commercially available surgical staple delivery systems; (2) must use the same materials, measurements, and spacing of existing surgical staples; (3) must be deliverable using currently available surgical stapling instruments; (4) must be easily assembled into the stapler cartridge and be readily sterilized; and (5) must be deliverable with minimal radiation exposure to the physician and other operating-room personnel.

The proposed source/staple was designed such that it could be easily assembled into the cartridge of a surgical stapling device, which can accommodate staples with diameter up to

0.5 mm. A standard surgical staple fabricated with titanium wires, measuring 0.21–0.28 mm in diameter, 3–4 mm in width, and 2.5–4.8 mm in length was used as a template (Fig. 1).

Construction

A titanium tube 0.28-mm inside diameter was constructed to contain the source, which measures 1.25 mm in length. The radioactive material ^{169}Yb was sealed within the titanium tube and then capped and resealed by titanium wires laser welded to the tube to serve as the legs of a tissue-fastening system. The ^{169}Yb staple measures 3.0 mm in length and 0.40 mm at widest dimension (Figs. 2A and 2B).

The source/staple will be loaded into a specially fabricated staple cartridge constructed of high-density plastics combined with high atomic number (high-Z) material (i.e., tungsten), designed to provide shielding to operating-room personnel during insertion. Relatively minimal shielding is required for ^{169}Yb , with a half-value layer in tungsten-impregnated plastic of 0.33 mm and corresponding tenth-value layer of 2.4 mm.

Dosimetry calculations

Brachytherapy sources are generally characterized in accordance with the recommendations of the updated American Association of Physicists in Medicine (AAPM) Task Group Report No. 43 (TG-43U1) (15, 16). This characterization is fundamentally based on the assumption of axial symmetry of the source. As shown in Fig. 2A, this staple is not axially symmetric; the deployed staple legs cause a perturbation of the axial dose distribution. Although a full report of the source dosimetry in accordance with AAPM TG-43U1 is outside the scope of this article, we evaluated this perturbation of the axial dose distribution for the ^{169}Yb staple and compared this with a staple using ^{125}I .

A Monte Carlo calculation of the axial dose perturbation was made. An ^{169}Yb source was modeled in a Monte Carlo N-Particle Transport Code 5 (MCNP5) environment using the material specifications described earlier. The source construction was nonsymmetric about the coaxial axis but symmetric about the transverse plane.

Radiation transport calculations were performed on a Windows-based personal computer running the MCNP5 Monte Carlo computer code (17). This computer code was used to simulate coupled photon and electron transport through material using the nondefault Monte Carlo Photon Library (MCPLIB) 04 photo-atomic cross-section tables provided with the MCNP5 code. These cross-section tables, derived from the Evaluated Photon Data Library 97 data set (18), were used in place of the default MCPLIB01 cross-section tables because of their superior representation of low-energy photoelectric interactions in low-Z materials (19–21). Simulations were performed in water computer models with a total of 2×10^8 source photon histories processed for each simulation. Highly complex photon spectrum of ^{169}Yb (22) included 73 gamma ray and five X-ray emission lines. One gamma ray (8.41 keV) and one X-ray (7.18 keV) were omitted from the model, because the transmission of these photons through the 0.06-mm titanium shell was negligible. The MCNP code simulated a uniform activity distribution within the source.

The source was placed at the center of a 40-cm water phantom. This phantom size was selected, because it approximates an infinite water phantom for the more energetic photon spectrum of iridium-192 (23). Dosimetric data were determined at a radial distance of 10 mm over polar angles ranging from 0° to 180° and axial angles ranging from 0° to 360° using the MCNP5 *F4MESH tally multiplied by its respective mass–energy transfer coefficient, μ_{tr}/ρ (cm^2/g) for water, to obtain the water kerma per source photon (MeV/g /photon). The same methodology was used for the analysis of ^{125}I by substituting the Yb pellet with a quartz pellet coated with ^{125}I and substituting the ^{125}I photon spectrum.

Use of sources

Surgical staplers used for VATS are typically loaded with cartridges containing multiple staples so as to place two, triple-staggered rows of staples with 1 mm between the edges of adjacent staples, thereby creating a geometrically rigid surgical staple line ideal for the delivery of permanent brachytherapy (Fig. 3).

A staple sidecar was designed to attach to the head of commercially available staplers used for the VATS procedure (Fig. 4A). Any available cavity within the surgical stapler itself or within the sidecar could accommodate ^{169}Yb source staples. Typically, the surgical stapler is loaded with a cartridge containing standard surgical staples and the sidecar with a cartridge containing the source staples. The sidecar design allows for the placement of biologically active staples at a fixed distance from the suture staple margin (Fig. 4B).

Results

Structural integrity

To test the integrity of the source/staple, tensile tests were performed to ensure that the creation of a capsule containing the ^{169}Yb with the attached leg fasteners did not reduce the tensile strength. Test source capsules were subjected to a tensile load to failure. In each test source, failure occurred in the wire of the fastener leg, and there were no weld failures (Fig. 5). The tensile test was performed on a total of five source/staples to assure the replication of the fastener leg failures. The tensile load producing failure was 6.5–7.5 lbs (29–33 newtons), which exceeds the yield strength of standard surgical staples.

Use of sources

Placement of source/staples using a commercially available surgical stapler was mimicked in a tissue phantom (Fig. 6).

Dosimetry

The results of the Monte Carlo calculation of the dose distribution surrounding the ^{169}Yb source, normalized to the dose at a distance of 10 mm on the transverse axis of the source, are presented in Fig. 7A. Similarly, the Monte Carlo results for the ^{125}I source are presented in Fig. 7B.

Monte Carlo simulations at 10 mm from the source staple in the plane containing the legs of the staple and in the perpendicular plane demonstrated that perturbation by the source legs was most prominent at the oblique angles of the longitudinal plane. The percent dose perturbation was calculated to be 4–5% for ^{169}Yb as compared with 32% for ^{125}I (Figs. 7A and 7B). Both dose modeling and measurement showed that the anisotropy results from the ^{169}Yb source were significantly more favorable than those resulting from a similarly designed ^{125}I source.

Evaluation of dose distribution

Given the predictable geometry of implanted sources delivered by the stapler sidecar, treatment planning can be done easily using any treatment planning system that calculates based on AAPM TG-43U1 parameters (e.g., PLATO (Nucletron, Veenendaal, the Netherlands)). With a half-life of 32 days and an initial activity of 2 mCi, a single permanently implanted ^{169}Yb staple will deliver approximately 43 Gy to any single point located perpendicularly 1 cm from the source. The implanted sources may contain up to 5 mCi of ^{169}Yb (typical load of 2 mCi) to deliver a dose of 125–140 Gy to the resection

margin, located 8 mm–1 cm from the source. The number of seeds implanted is dependent on the length of the resection margin.

Discussion

With higher photon energies, ^{169}Yb results in less dose perturbation in the clinical target than would result from an ^{125}I source in this configuration. The anisotropy calculations presented earlier highlight the advantages of using this intermediate photon energy source, particularly, in a source/staple comprising a titanium tube and titanium wires. Comparisons of dose homogeneity in interstitial implants favor ^{169}Yb over ^{125}I (11). Moreover, with low half-value and tenth-value layers, ^{169}Yb requires only minimal shielding on the order of millimeters, allowing a cartridge composed of high-density plastic containing high-Z material to provide sufficient shielding for physicians and operating-room personnel.

Widespread application of brachytherapy in conjunction with wedge resection in the treatment of early-stage lung cancer has been hampered because of the limitations associated with currently available radioactive seed delivery systems. Several intraoperative brachytherapy techniques have been reported.

Pisch *et al.* (24) described the use of loose seeds manually delivered by means of a Mick applicator (Mick Radio-Nuclear Instruments Inc., Mount Vernon, NY). The challenges inherent in this procedure include the multiple needle passes that are required through the lung parenchyma, the risk of uncontrolled seed migration, the impracticality of implementation through a thoracoscopy port, and nonapplicability in most patients with chronic obstructive pulmonary disease. The proposed novel brachytherapy source has been designed especially for compatibility with VATS. The construction of the source within a staple provides inherent fastening to tissue, thereby eliminating the risk of seed migration.

Lee *et al.* (8) have described a technique using commercially available strands of ^{125}I seeds that are embedded in polyglactin 910 suture. Through an open thoracotomy incision, these suture seeds were sewn along the residual lung tissue after wedge resection, resulting in highly reproducible placement of sources along the resection margin. However, this technique may be associated with high radiation exposure to operating-room personnel and unpredictability of final dosimetry after reexpansion of the lung. The proposed novel brachytherapy source would be loaded into a shielded cartridge as discussed earlier, limiting the dose to the hands of physicians.

To address many of these issues inherent in “free seed” placement, Chen *et al.* (7) developed an intraoperative technique using vicryl mesh imbedded with ^{125}I radioactive seeds for thoroscopic placement over the tumor bed and staple line after a VATS resection. This technique has been shown to allow for very little radiation exposure to physicians and staff during implantation (25). However, the primary limitation of this technique was that the desired dose distribution was entirely dependent on proper positioning of the mesh in relation to the target tissue, because the seeds are secured to the mesh before insertion. Careful suturing of the platform is essential to prevent the migration of the mesh from the suture line on reinflation of the lung. Such migration, which may occur anywhere along the suture margin, renders it difficult to affix the mesh at a suitable distance from the cut lung margin for the entire length of concern. In contrast, when using a sidecar attached to a commercially available stapler head, biologically active ^{169}Yb seeds are used simultaneously and at a fixed distance from the surgical staples defining the suture margin. Moreover, the proposed technique allows for adaptable and dynamic planning in the operating room; additional staples may be added as needed to cover the entire length of extended resection margins.

Pisch *et al.* (26) have reported on the feasibility of using the da Vinci robotic surgical system for seed placement in the wedge resection margin, but the complexity and expense of this robot are likely to limit its widespread implementation.

The limitation inherent in each of these systems has prompted us to develop a framework around which the brachytherapy source–delivery could be optimized. We have designed and fabricated an isotopic source that is directly incorporated into the surgical staples used for wedge resection. In this way, the sources are secured in a rigid position directly adjacent to the surgical resection edge. They can be readily placed through a minimally invasive surgical incision and can be delivered to the pulmonary parenchyma by means of the VATS work port, resulting in minimal exposure to operating-room staff. The seed positions will be rigidly fixed, assuring that the dose distribution will not be perturbed by lung reinflation or allow for uncontrolled seed migration during the course of treatment. This source–delivery system permits dose distribution to be effectively preplanned before surgery for optimal placement and easily adjusted to compensate for the ultimate surgical resection margin length. This source–delivery system design can be readily implemented with existing surgical stapling products.

Conclusion

We have developed a ^{169}Yb brachytherapy source and delivery system that can be used in conjunction with any commercially available surgical stapling instrument, facilitates the precise placement of brachytherapy sources relative to the surgical margin, assures that the seeds remain fixed in their precise position for the duration of treatment, overcomes the technical difficulties of manipulating the seeds through the narrow surgical incision associated with VATS, and reduces the radiation dose to the clinicians.

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Fig. 1.

Schematic representation of a standard surgical staple used in conjunction with commercially available surgical stapling instruments widely used for video-assisted thoracoscopic surgery.

Fig. 2. Illustrated representation of ytterbium-169 source staple with radioactive element sealed within a titanium tube that is laser welded to titanium wires (A) and source/staple as compared with a normal surgical staple (B).

Fig. 3. Schematic representation of the staple pattern in a typical surgical stapling system (ENDO GI ROTICULATOR 45–3.5; manufactured by Auto Suture USSC, Norwalk, CT).

Fig. 4. Illustrated representation of “sidecar” delivery device attached to the head of a surgical stapler (A) and relative position of biologically active ytterbium-169 source/staples to surgical staples after deployment (B).

Fig. 5.
Source/staple subjected to tensile load to the point of failure. Failure occurred in the staple leg, not in the source tube or weld joints.

Fig. 6. Magnified view of source/staples placed in a tissue phantom (A) using commercially available surgical stapler widely used for video-assisted thoracoscopic surgery (B and C).

Fig. 7. Monte Carlo simulation of dose distribution for ytterbium-169 (A) and iodine-125 (B) at 1 cm from the source/staple in the plane containing the legs of the staple (y-z plane) and the plane perpendicular to the x-z plane.