

## ABSTRACT SECTION

### 1. Targeted Delivery of Chemotherapeutic Agents Using Improved Radiosensitive Liquid Core Microcapsules and Assessment of Their Antitumor Effect

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#### Purpose

Radiation-sensitive microcapsules composed of alginate and hyaluronic acid are being developed. We report the development of improved microcapsules that were prepared using calcium- and yttrium-induced polymerization. We previously reported on the combined antitumor effect of carboplatin-containing microcapsules and radiotherapy.

#### Methods and Materials

We mixed a 0.1% (wt/vol) solution of hyaluronic acid with a 0.2% alginate solution. Carboplatin (1 mg) and indocyanine green (12.5 µg) were added to this mixture, and the resultant material was used for capsule preparation. The capsules were prepared by spraying the material into a mixture containing a 4.34% CaCl<sub>2</sub> solution supplemented with 0–0.01% yttrium. These capsules were irradiated with single doses of 0.5, 1.0, 1.5, or 2 Gy 60Co  $\gamma$ -rays. Immediately after irradiation, the frequency of microcapsule decomposition was determined using a microparticle-induced X-ray emission camera. The amount of core content released was estimated by particle-induced X-ray emission and colorimetric

analysis with 0.25% indocyanine green. The antitumor effect of the combined therapy was determined by monitoring its effects on the diameter of an inoculated Meth A fibrosarcoma.

#### Results

Microcapsules that had been polymerized using a 4.34% CaCl<sub>2</sub> solution supplemented with  $5.0 \times 10^{-3}$ % (10-3% meant or 10%-3) yttrium exhibited the maximal decomposition, and the optimal release of core content occurred after 2-Gy irradiation. The microcapsules exhibited a synergistic antitumor effect combined with 2-Gy irradiation and were associated with reduced adverse effects.

#### Conclusion

The results of our study have shown that our liquid core microcapsules can be used in radiotherapy for targeted delivery of chemotherapeutic agents.

### 2. Image-Guided Radiotherapy in Near Real Time With Intensity-Modulated Radiotherapy Megavoltage Treatment Beam Imaging

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#### Purpose

To utilize image-guided radiotherapy (IGRT) in near real time by obtaining and evaluating the online positions of implanted fiducials from continuous electronic portal imaging device (EPID) imaging of prostate intensity-modulated radiotherapy (IMRT) delivery.

**Methods and Materials**

Upon initial setup using two orthogonal images, the three-dimensional (3D) positions of all implanted fiducial markers are obtained, and their expected two-dimensional (2D) locations in the beam's-eye-view (BEV) projection are calculated for each treatment field. During IMRT beam delivery, EPID images of the megavoltage treatment beam are acquired in cine mode and subsequently analyzed to locate 2D locations of fiducials in the BEV. Simultaneously, 3D positions are estimated according to the current EPID image, information from the setup portal images, and images acquired at other gantry angles (the completed treatment fields). The measured 2D and 3D positions of each fiducial are compared with their expected 2D and 3D setup positions, respectively. Any displacements larger than a predefined tolerance may

cause the treatment system to suspend the beam delivery and direct the therapists to reposition the patient.

**Results**

Phantom studies indicate that the accuracy of 2D BEV and 3D tracking are better than 1 mm and 1.4 mm, respectively. A total of 7330 images from prostate treatments were acquired and analyzed, showing a maximum 2D displacement of 6.7 mm and a maximum 3D displacement of 6.9 mm over 34 fractions.

**Conclusions**

This EPID-based, real-time IGRT method can be implemented on any external beam machine with portal imaging capabilities without purchasing any additional equipment, and there is no extra dose delivered to the patient.

