

Course: Tuesday, *Bringing Radiation Therapy to the Next Level*

Talk Title: Current Status of Radiotherapy – Is There A Need for (MR) Image-Guidance?

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Highlights

- **X-Ray CT guides modern intensity-modulated radiotherapy (IMRT). It enables 3D treatment planning and dosimetry.**
- **Adding MRI improves definition of normal and diseased anatomy. This enables improved segmentation, and more conformal treatment planning. MRI is routinely used for brain tumor treatment planning, and is often used for prostate cancer where it reveals precise gland boundaries.**
- **This talk will focus on the potential clinical benefits of new combined MR / XRT delivery systems for “Adaptive Radiotherapy”. By enabling MRI with every fraction, these systems have potential to compensate for complex motion of the target, and surrounding anatomic structures, including real-time motion tracking**
- **Work is still needed on MRI-only dosimetry, real-time MR-based segmentation and treatment planning, and outcomes research linking MR-guidance to reductions in complications and treatment failures.**

Target Audience: Physicists, Engineers, Radiotherapists and Radiologists involved in radiation therapy

Problems with standard radiotherapy.

Modern radiotherapy uses geometrically converging external high energy beams that deliver a high dose of ionizing radiation that conforms to a desired target region (the CTV or “clinical target volume”), while dose to non-target tissues is minimized. Multiple treatment sessions or “fractions” are used to accumulate high, lethal doses at the target. Brachytherapy uses multiple radiation sources that are permanently or temporarily inserted into the target region. Optimal dosimetry relies on careful placement of these sources.

Radiotherapy treatment failures include tumor recurrences due to inadequate dose delivery to the target lesion, and adverse effects due to excessive dose delivery to radio-sensitive organs. Recurrences after radiotherapy include both local recurrences at or near the margins of this initial target, as well as distant “systemic” recurrences (i.e. metastasis). Local recurrences result from insufficient dose to the target either because the planned dose was insufficient or was not achieved during the treatment. Inadequate dose planning can occur because the target tumor is radiation resistant (i.e. hypoxic, etc), or more commonly because occult microscopic disease that cannot be identified on treatment planning scans extends beyond the CTV. Inadequate dose delivery can occur because the position and/or shape of the target moves away from the initial planned region during or between serial dose fractions. Metastatic disease spreads from residual inadequately treated disease in some cases. In other cases microscopic metastases may be present but clinically occult at the time of initial therapy. In most cancer treatment plans the gross tumor volume (GTV) is dilated by up to 2 cm resulting in a CTV that includes a margin where residual microscopic disease is likely to be treated. Then, the CTV is dilated slightly further yielding a planned treatment volume (PTV) that accommodates potential inaccuracies due to motion, etc.

Adverse effects after radiotherapy are primarily local and arise from immediate and long term radiation damage to structures with critical functions near the target. (Systemic effects such as immune suppression are rare with modern conformal therapy). Adverse effects may occur because critical structures are intimately associated with target lesion, and cannot be fully excluded from significant dose despite optimal treatment planning, or because critical structures inadvertently move into higher dose regions during treatment(s). Adverse effects vary by target location. Examples of “expected” adverse

effects include erectile dysfunction after prostate radiotherapy and xerostomia (reduced saliva) after oropharyngeal radiotherapy. Examples of complications include rectal bleeding after prostate radiotherapy.

Motion is thus one significant cause of both treatment failures and adverse effects. Patient-specific cradles and masks, and external fiducials are commonly used to limit motion between and during fractions. Many LINAC gantries can also perform “cone-beam” 3D CT immediately prior to each fraction to assess and correct position deviations. Small fiducials can even be physically inserted into target organs that have a high risk of bulk motion, such as the prostate, and tracked during treatment by x-ray fluoroscopy (for gold seeds), or rf tracking systems (for active fiducials). These methods enable “Adaptive” radiation therapy in which dose is frequently readjusted to match motion.

Potential technical benefits of MRI-guidance that address limitations of CT-guidance

MRI provides clear benefits for initial treatment planning because of its superior soft-tissue visualization of pathologic targets as well as critical normal structures. MRI (including MRSI) (as well as other modalities such as PET/CT) is well established and routinely fused with standard 3D CT to improve CTV definition in the brain and head and neck, and is commonly used in some centers for prostate definition as well. This is despite obstacles to MR imaging analysis such as spatial distortions due to gradient linearities or eddy currents, and signal variations due to coil sensitivities, and non-isotropic noise that pose challenges to semi-automated image analysis. MRI’s ability to more clearly define the GTV has also enabled plans that include a “boost” of additional dose to the most worrisome part of the GTV in hopes of further reducing the local recurrences.

The emerging integration of MRI into radiotherapy delivery systems offers unique improvements over existing cone-beam and fiducial tracking systems, including improved non-rigid volumetric tracking of complex motion such as peristalsis and respiration that not only affect the target position but the configuration of nearby critical structures as well for even more precise, “online” adaptive radiation therapy. MRI also offers the opportunity to tailor treatment plans as tumors and normal structures shrink or change shape over the course of multiple fractions.

Clinical Opportunities for MR-guided – selected examples

Head and neck cancer. Two common issues in head and neck radiotherapy are the dramatic shrinkage that can occur during the course of therapy, and poor ability to distinguish confluent target nodal masses from normal structures. The neck is also difficult to reproducibly immobilize with external fixation. Thus head and neck cancer has been identified as an ideal target for “online” adaptive radiotherapy in which imaging is repeated with each fraction [2].

Prostate cancer. The close proximity of the rectum, and the variable size and position of the rectum leads to significant non-reproducible motion of the prostate. Furthermore, non-contrast CT has limited definition of the prostate boundaries. While motion of the prostate can be tracked with fiducials, MRI offers the potential for volumetric tracking, an tracking of the adjacent rectum and bladder base. MRI also has potential to demonstrate clinically significant dominant foci of tumor, which can be used to define a target volume for additional dose boost [3] or, in the case of limited disease, for focal therapy [4].

Head and neck cancer. Tumor shrinkage and weightloss during treatment for head and neck cancer can lead to marked anatomic changes in anatomy during the course of multiple fractions. Repeated replanning (adaptive IMRT) is being investigated in these patients [5]. MRI has potential to improve this process by facilitating better soft tissue discrimination of relevant anatomy.

Pancreatic and biliary tumors. Respiratory motion causes periodic motion of upper abdominal structures. Fiducials have been used to track motion, but non-rigid motion is particularly problematic in organs with variable attachment to the stationary retroperitoneum and the moving diaphragm including liver. Volumetric tracking with MRI has potential to enable more precise treatment plans, especially near sensitive structures such as colon, stomach and heart [6].

Challenges for realtime MR-guided adaptive radiation therapy.

Rapid bone segmentation & dosimetry. MR-only treatment planning would facilitate adaptive IMRT but manual segmentation of the bones must be automated [7]

Rapid soft tissue and target segmentation. Tools that can accommodate the spatial signal variations of MRI, must be fast and efficient, and even real-time if used to track volumetric motion in lieu of fiducials. MRI navigators could facilitate this process.

Imaging coils. Most MRI is performed with surface coils that contain radio-dense metal components that may interfere with dosimetry, and may not be hardened to high dose ionizing radiation.

Fast, 3D scanning. Many diagnostic MRI scans are performed with exams that take up to 1 hour, use intravenous contrast, functional tasks, and or 2D thick slices to provide optimal target visualization. Others, such as diffusion-weighted imaging with EPI, suffer from non-linear spatial distortions in regions of B0 inhomogeneity, such as near bowel. These must be overcome for their effective use in therapy planning.

Cost

Constraints on delivery systems. Even with split magnet designs, there are reduced geometric ports available using MRI-guide IMRT compared to some un-encumbered systems such as pencil beam linacs that deliver radiation from a very wide range of solid angles. Also, the energies available from some radioactive source systems are not equivalent to modern LINACs. This may have potential effects on achievable dosimetry.

What will learners be able to do differently because of this information?

The goal of the talk is to present background material that learners can use when planning studies on the design and use of MRI-guidance systems for radiotherapy.

References:

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