Rotationally Symmetric Patient Dose Perturbation in Radiotherapy of Cancer

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Course: PHY 3090U – Material Science

Date: Sunday March 22nd 2015

Researchers reduce unwanted external magnetic fields and dose perturbations in cancer radiotherapy by using a rotationally symmetric modality.

Researchers in the Department of Medical Physics at The University of Wisconsin have recently developed a new way to administer clinical dose volumes to patients during magnetic resonance (MR) image guided radiotherapy for reducing tumors. While radiotherapy is currently used to treat several forms of cancer, the group chose to evaluate clinical results for the lungs, prostate, and head and neck. This particular paper, published in *The International Journal of Medical Physics Research and Practice* (Medical Physics **42**, 715(2015)), is the first to show that a rotational symmetric administration of dose to tumor targets can effectively reduce the negative effects of external magnetic fields.

Current treatment of several forms of cancer relies on the use of radioactive sources such as Co^{60} to target the tumors and cause apoptosis. To ensure accuracy in detection and treatment, physicist determine the location of the tumor using magnetic resonance imaging (MRI) before and during treatment. And while alternatives such as chemotherapy in combination with photoacoustic imaging and ultrasound methods exist, radiation therapy stands as the benchmark of cancer treatment.

A major issue that radiation treatment and MR imaging must deal with today is the influence of external magnetic field on dose distributions to the patient. Though the (primary) photon beam administered will be applied linearly, neighboring Lorentz forces deflect secondary particles in a circular fashion around the magnetic field lines, resulting in hot spots of excess dose. The resulting fluctuation in dose perturbation can render radiation treatment plans both unsafe and inaccurate, and so an efficient solution is necessary. The recent research efforts of Dr. Bryan Bednarz, an Assistant Professor in Medical Physics and Human Oncology at the University of Wisconsin might have just found the solution. Dr. Bednarz group seeks to develop novel Monte Carlo (MC) simulations for radiation treatment administered by photon beams. This paper in particular was produced by the efforts of first author and current doctorate student You Ming Yang. While speaking with Yang, his enthusiasm to push the limits of in computational modelling and cancer treatment was clear. When I asked him about the reasoning behind the use of the rotational model, he cited a few key points. “The linear models result in an increase in exit dose due to ERE’s (electron return effect, which may be mitigated by a skin bolus), and an asymmetric shift of the dose penumbra relative to the beam penumbra. Rather than using a few discrete beams with well-defined penumbra, rotational modalities effectively give a ‘smear’ of beams that results in an infinite number of lower-intensity beams (so smaller dose penumbra perturbation), while also allowing the possibility for infinite number of opposing beams from the other direction.”

To better understand the ingenuity of Yang’s results, once must have a little background on radiotherapy. Radiation treatment uses ionizing radiation to treat the cancer by damaging the DNA of cancerous tissue to induce cell death. To ensure that the normal cells are also not completely targeted, several radiation beams are applied at different angles to intersect at the tumor, resulting in larger absorption of administered dose in the targeted area. In the clinic, the patient is placed in a bed directly beneath a guiding system and electron gun. During imaging, a magnetic field 30,000 times stronger than that of Earth surrounds the body, causing nuclei in body tissue to align with the magnetic field and vibrate with a specific frequency. The scanner subsequently transmits radio-frequency signals to nuclei in the part of the body being imaged, allowing for change in alignment for the specific area. Once the field is turned off, the nuclei realign themselves in the direction of the magnetic field and the scanner (with the help of a computer) characterizes the body tissue by the strength and duration of the signal, producing 2D and 3D images.

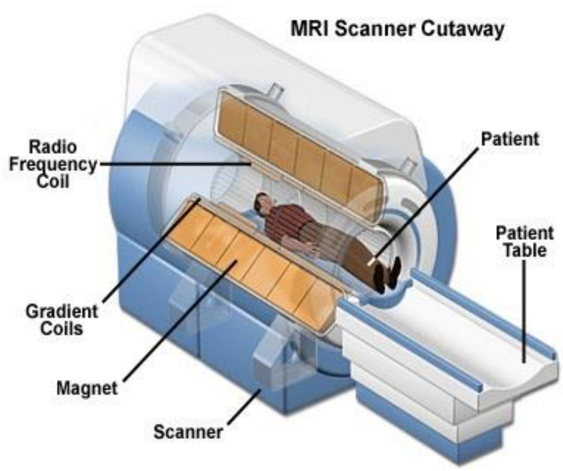

Figure 1: Cutaway of an MRI scanner used to image the patient’s tumor

Next, once radiation oncologist (medical doctors that specialize in cancer treatment) know the tumor's location with a high degree of accuracy, several radiation beams intersect at the tumor. In the model tested by Yang and his colleagues, rather than employing linearly accelerated beams (LINAC) intersecting from different angles, a device attached to the image guiding system will rotate around the bed where the patient lies, cancelling any external magnetic field present. The dose heterogeneity index for the helical trajectories, which is used to measure the variation in target dose volumes and those predicted, results from the liberated charged particles created by the transverse magnetic field; It is given by:

$$DHI = 100\ x\,\frac{D_{20} - D_{80}}{D_{pres}}$$

D_{20} and D_{80} are the minimum doses to 20% and 80% of the target volume, and D_{pres} is the prescribed dose. The larger the DHI value, the greater the dose heterogeneity in the target volume.

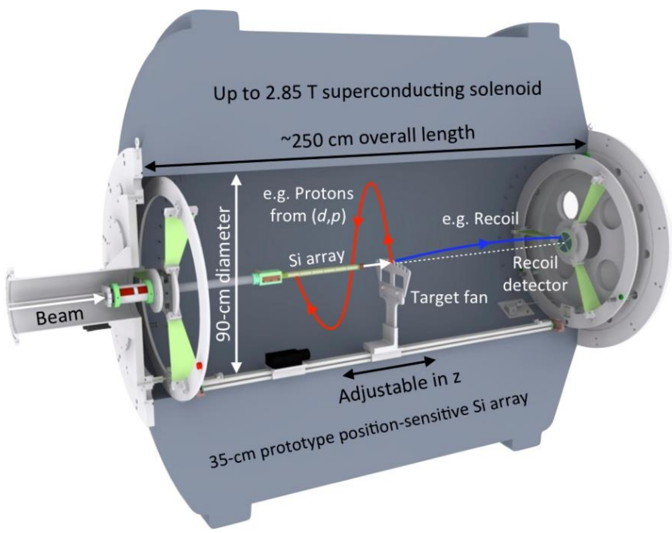

Figure 2: General schematic of particle beam fired through superconducting solenoid to treat patient during radiotherapy

An underappreciated part of the studies performed is the use of a phantom: a constructed box created to replicate the conditions of the tissue that will eventually be treated. The material the phantom is made of often varies, with different materials offering different advantages and disadvantages; in this study, a simple homogenous slab phantom was used to record results. This particular phantom was composed of alternating layers of air, water, and tissue to simulate the particle beam going through air, interacting with the water (that simulates tissue very well), and then through the particular tissue of focus. For example, the lungs are less dense then human body tissue such as skin (1 g/cm^3), so a uniform mixture of density 0.2 g/cm^3 was added as a semi-infinite layer into the phantom for more accurate simulation. Some research groups choose to even create a replica of the tissue to be targeted (e.g. larynx), but Yang's reason for using a slab phantom was quite simple: If the shape of the phantom can be simple, then benchmarking certain physical parameters and using key effects while also comparing them to previous literature can be made easy. In addition, slab phantoms offer a high degree of symmetry, so only one direction of the magnetic field and other effects need to be considered, as the x and y axis are semi-infinite. In other words, since the beam is oriented in one direction and the magnetic field is oriented in one direction, then all of the effects (e.g. depth dose, profile changes) occur in only one direction.

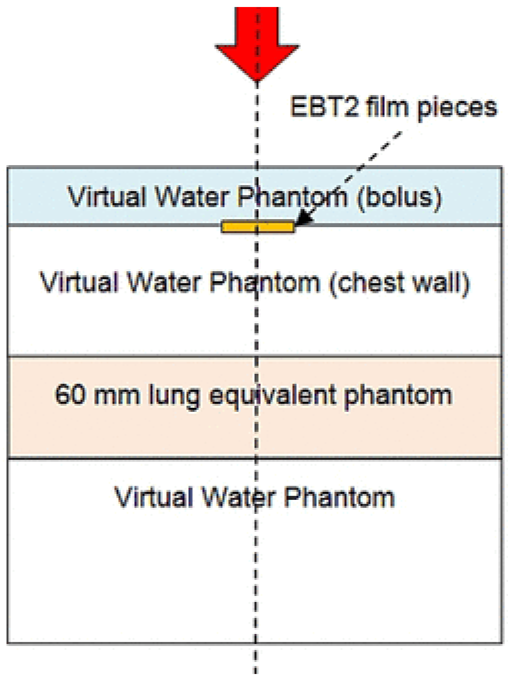

Figure 3: Layers of simple slab phantom for the lung case. In other words, this phantom is the water equivalent setup with a lung equivalent phantom and a bolus-simulated layer.

Before the dose is administered, computational models are created to provide statistical data for treatment prior to it being given. The MC code used by Yang was GEANT4, a toolkit commonly used in the field for the simulation of the passage of particles through the body, producing accurate treatment plan beamlet and patient configurations. While commonly used in medical physics research, GEANT4 is also used for high energy simulations, and space science. A set of sample codes used for medical physics applications can be found here.

The results for the simulations performed by Yang and his coworkers were excellent for prostate and head and neck simulations. The dose differences from actual and expected were only ± 3 Gy (Gy for gray, the SI unit for radiation dose), since the electrons in the air aimed at the tissue were only confined to spiral helices along the magnetic field lines, parallel to the patient axis and thus confined only to the region where the tissue is. The lungs on the other hand were most noticeably affected by the transverse magnetic field, resulting in significant perturbations of the overall dose delivered. The reason that the prostate results showed no significant dependence on the magnetic field strength was because the prostate has a relatively homogeneous geometry, where only the hip bones are the closest bone structures. The symmetric incident beam will in turn produce a localized radiation distribution, and so the resulting dose heterogeneity index values for all the field strengths tested are relatively low (3.0%). Likewise, the results for the head and neck are very close to expected, even though there is a more heterogeneous geometry due to the bones and surrounding air pockets. Furthermore, the high density of tissue in this region does not allow for the Lorentz force to play much of a role, so an overall DHI for the magnetic fields tested is approximately 5.3%. Conversely, the results for the lung have the greatest influence by the transverse magnetic field. This is because the lungs are always moving and for there to be any consistent dose given to the lungs, the patient must hold their breath consistenly for the entire duration of the lengthy therapy. This results in the tumor position in the mostly heterogeneous lungs to vary, so the margin is quite large and the low density of the lungs allows the Lorentz force dose perturbations to play a larger role

While talking with Yang, he spoke of how the next steps to the project will aim to create a generalized Monte Carlo based treatment planning optimization platform. He also indicated that plans of building on the original project were to create an optimization platform for the new ViewRay device used for the experiment (MR Image guided radiation therapy device that uses 3 cobalt sources), but due to very busy corporate presence in the hospital, the project could not be continued for further research on different tumors.

Summary for use in RSS Feeds

The integration of magnetic resonance image guidance with radiotherapy to reduce tumor position uncertainty during photon radiotherapy is a progressively sought after goal for many research groups. While the reduction of tumor by radiotherapy is favorable, magnetic field-induced dose perturbations can cause tumor position uncertainty and neither appreciated or accounted for. Researchers at the University of Wisconsin's Medical Physics department propose a solution to this unwanted effect by using a rotationally symmetric modality like helical Tomotherapy that will allow effective reduction of these dose perturbations. The study shows that for the three clinical treatment plans examined (head and neck, prostate, and lung), the clinical dose-volume histograms are 4% within the dose agreement for the target volumes, demonstrating the mitigation of external magnetic fields by a rotationally symmetric treatment modality.

Interview Transcript with You Ming Yang

March 18th 2015 (full audio available in mp3 file)

1) **How did you figure out using a rotational model compared to other ones available?**

Previous works in literature (Kirkby 2008, 2010, Raaymakers Netherlands), which evaluated MRIgRT in fixed gantry IMRT configurations showed two main dose perturbations (for what are called perpendicular beam geometries):

1) An increase in exit dose due to EREs (which may be mitigated by a skin bolus)
2) Asymmetric shift of the dose penumbra relative to the beam penumbra. The Asymmetry being due to the right handedness of the Lorentz force, and the latter of which could be somewhat mitigated by using opposed beams, a method that 1. Isn't perfect due to beam divergence, and 2. It isn't always ideal for IMRT (non-opposing beam imrt can offer better sparing and coverage)

Rotational modalities are somewhat of an extreme extension of the opposed beam concept. Rather than using a few discrete beams with well-defined penumbra, rotational modalities effectively give a "smear" of beamlets, resulting in not only an infinite number of lower-intensity beamlets (meaning smaller dose penumbra perturbation), but also allow possibility for infinite number of opposing beamlets from the other direction.

2) **Why did you choose to specifically look at lung, prostate, and head and neck only for cancer treatment?**

We chose these three cases because they somewhat representatively span the basis space of what you'd encounter in patient geometries.

1) The prostate is a relatively homogeneous geometry with a very symmetric incident fluence, and a very localized PTV.
2) HN (head and neck) has a more heterogeneous geometry (bones, distributed PTV, air pockets etc.), but high density of tissue doesn't allow for the Lorentz force to play much of a role.
3) Lung is most heterogeneous, and the low density lung material allows the Lorentz force dose perturbations to play a larger role.

3) **What material is the slab phantom made of? Why didn't you choose to make a replica of the organ (e.g. lungs) for the phantom?**

The simple slab phantom was homogeneous with a layer of water, air, and material of density equivalent to the tissue being examined (e.g. 0.2 g/cm^3 for lung), followed by another two layers of air and water. All three phantoms were anonymized patient CTs, reproduced in Monte Carlo.

4) **What advantages does radiation therapy offer over a treatment technique like ultrasound?**

My expertise in ultrasound based therapy is limited, but If you are referring to ablative ultrasound, the reason is part historical and part technological the use of radiation in medicine is over 100 years old, and we used isotopes back then, where radiation from decays were used for imaging, for skin treatments, etc. Furthermore, radiation is very penetrating (exponential decay at ~MV energies like cobalt, which was widely available after World War 2), so we get effectively an infinite range (albeit with exponential attenuation), but still well defined behavior in body.

Ultrasound transducers are capable of generating coherent waves capable of ablation are a relatively new technology. Additionally, ultrasound cannot penetrate bone (something we try to avoid in RT, but for example in Stereotactical radiosurgery, going through skull, ultrasound would heat skull)

5) **I understand that you used the TomoPen code for your simulations. Can you tell me a little bit more about that?**

TomoPen is the work of doctor Edmond Sterpin, refer to his papers for full details. Basically raw phase space simulated, then analytically attenuated through mlcs.

6) **What do you mean when you say for the lung case (page 5 of 12, second last paragraph):**

" periodic motion of the lung and target within a large low-density region can be more precisely and directly tracked with MR image guidance, but it involves the worst dosimetric configuration with low density that enhances the range of the spiraling charged particles "

I.e. why the lung case is the most important treatment and not another (e.g. head and neck)?

The goal of MRIgRT is to offer real-time image guidance. The most common way of performing IMRT is to scan the patient one day (with immobilization devices, cage for head, balloon inserted up rectum and inflated for prostate, empty bladder, etc.). For the lung, the patient must hold their breath and markers placed outside of the body are often used, but tumor position in lung can vary, so the margin is quite large. In general, there are three steps that must be taken in radiation therapy: (1) Plan and account for a margin for setup uncertainty; (2) Generate the plan itself; (3) Scan the patient for any gross changes day of, and treat if acceptable.

MRIgRT allows reduction of margins because real-time imaging lowers setup uncertainty for all cases, and especially in lung, where rather than going by a marker at chest height, you get a real time image of the tumor. However the low density of the lung means the electrons can spiral much further before stopping, meaning they can deviate more from their path

7) **When creating skin contours to evaluate skin dose perturbations, are lesions and scars in the skin ever taken into account?**

I can't speak specifically to this, as it most likely varies on a case by case, but radiation does also damage normal tissue, and slow down healing of lesions, scars, surgical incisions etc. If there is a region to be avoided, its relative sensitivity to radiation would be assessed, and assigned a certain importance factor relative to all the other "organs at risk", as well as the importance factor of the tumor. Then a radiation plan would be generated by the computer, and if necessary, evaluated and re-planned.

8) **Is there any reason for the dose distributions for the prostate plan showing no significant dependence on magnetic field strength?**

The symmetry of the original plan for the prostate, and the uniformity of the patient body allowed for a natural cancellation of the majority of the effects of the asymmetric Lorentz force. Additionally, the relatively

9) Are there any plans on building on the research done here (e.g. different tumors, image quality)? What is the current project you are working on?

Originally create optimization platform for our new ViewRay device (MRIgRT device using 3 cobalt sources), but difficulty in obtaining details from a very busy corporate entity, shifted gears. Working on a generalized Monte Carlo based treatment planning optimization platform

10) Why did you choose to go into the field of medical physics?

I was originally a plasma physicist and interested in fusion energy. The grandiose goal of infinite energy (deuterium in the ocean, enough energy to power world until sun expands and engulfs half the solar system), seemed great, but the dream has been 50 years away for the last 70 years. So there is always a new problem, and government interest has been waning, with researchers constantly begging for research funding. I then transferred to medical physics, which is much faster paced, has greater industry interest, and more funding to do research that gets applied quicker and helps more people.