I am James F. Dempsey, Ph.D., Nucl. Chem., developer of new weapons to fight cancer. My team solved "impossible" problems for treating cancer with radiation - while clearly seeing inside the patient - with a linear accelerator inside an MRI scanner, AMA!

James$_{D}empsey$[1]$andr/ScienceAMAs$[1]

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Abstract

The radiation treatment field has invested a lot of research into making better dose distributions and delivering accurately to patients. Many advances have been made in tracking breathing motion, surgically implanting marker or gels in the body, placing balloons in orifices to immobilize tissues, using X-Ray flat-panels detectors to find markers or make "cone-beam" CTs. However, all of these approaches still do not see the actual organs and tumor in real time as they move in the body during therapy. I founded ViewRay to solve this problem. MRI scanners provide the best soft tissue visual clarity of patients organs but they are not compatible with radiotherapy accelerators. People spent decades unsuccessfully trying to combine an MRI and a Radiation beam into a single, effective medically usefully device available to treat patients. In a sense, the MRI scanner and the accelerate do not like each other. The magnetic field generated by the MRI scanner can prevent the accelerator from operating and the accelerator uses radar technology and makes radiofrequency noise that can prevent the MRI from scanning clear images. So, we took a superconducting MRI and we split it in half opening it up, leaving the imaging volume floating in the middle where we could shoot in radiation beams while scanning. We created magnetic sleeves that could create voids in the magnetic field to protect the accelerator. Then we borrowed ideas from stealth aircraft to absorb the radiofrequency noise and eliminate it. Finally, we developed advanced software to compute and optimize dose, as well as, track tissues with real-time MRI video . This allows us to optimize, reshape, and track moving tissues so we do not miss, which is important to eradicate the tumor and spare healthy tissues. What we call the MRIdian® Linac system was FDA cleared in February of 2017. The MRIdian® an earlier generation system has been treating patients for over 3.5 years and data published at ASTRO 2017 showed significant early results in treating pancreatic cancer, known to be one of the most difficult cancers to effectively treat. http://www.viewray.com/press-releases/early-clinical-data-suggests-prolonged-median-survival-pancreatic-cancer I'll be back at 1 pm ET to answer your questions, Ask Me Anything. EDIT: Thank you /r/science mods and all the redditors that asked very good questions about MR image-guided RT. We'll check back later to see if there's any late questions.

the WINNOWER

REDDIT

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JAMES_DEMPSEY R/SCIENCE

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CORRESPONDENCE:

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Thank you very much for taking to time to do an AMA! I would appreciate any comments you have on some of my questions:

- The success with dose escalation using the Viewray system has been quite promising, particularly in pancreatic cancer as you point out. Do you feel that the reduced penumbra from moving away from Co60 sources will further improve your ability to reach BEDs greater than 100 Gy?
- Your competitor (Elekta) will be coming online with their MR-Linac shortly. Without starting a fight, what do you see as the comparative strengths of the Viewray system? The difference that's obvious to me is the magnetic field strength, 0.345 T vs 1.5 T in the Unity. Ostensibly, this would allow you to

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image with a higher frame-rate, however it appears that thus far your systems have been limited to 4 Hz. Will this be increased? If so, do you plan on using this increase to enable orthogonal slices? Having paired sag/cor would likely improve your target localization when the target drifts out of the sagital slice.

- Does 0.345 T provide sufficient SNR to perform diffusion weighted imaging in a reasonable time-frame, in order to better guide clinical adaptation decisions?
- What has Viewray been doing to address the contouring/adaptive planning time constraint hurdle? Have you been looking into machine learning to increase the speed of adaptation? I imagine that if your partner sites consented to provide you data, you would have a sufficiently large training set to make progress with this approach.

Edit: hurtle changed to hurdle

redoran

The MRIdian MR-Linac has a multi-leaf collimator with increased resolution to generate smaller beams and sharper penumbra. We do believe smaller, sharper beams will enable physicians to develop plans with higher conformality and better organ at risk sparing. These plan characteristics along with on-table adaptive replanning potentially allow for delivery of higher radiation doses. #2 - That's correct, the current frame rate is 4 frames per second (FPS). At the ASTRO meeting this year we showed a new imaging breakthrough under development where we took the 4 FPS imaging and doubled the FPS, while simultaneously doubling the SNR, and tripled the resolution. Before our breakthrough, a similar enhancement of fast imaging would require a 4 Tesla MRI. Of course a 4 Tesla MRI would have severe interactions with the radiation beam. We currently support 1 plane at 4 FPS or 3 planes for tracking at 1/2 the frame rate. #3 Yes. Please see these peer reviewed publications ->Distortion-free diffusion MRI using an MRI-guided Tri-Cobalt 60 radiotherapy system: Sequence verification and preliminary clinical experience. Gao Y, Han F, Zhou Z, Cao M, Kaprealian T, Kamrava M, Wang C, Neylon J, Low DA, Yang Y, Hu P. Med Phys. 2017 Oct;44(10):5357-5366. doi: 10.1002/mp.12465. Epub 2017 Aug 12. PMID: 28692129

Longitudinal diffusion MRI for treatment response assessment: Preliminary experience using an MRI-guided tri-cobalt 60 radiotherapy system. Yang Y, Cao M, Sheng K, Gao Y, Chen A, Kamrava M, Lee P, Agazaryan N, Lamb J, Thomas D, Low D, Hu P. Med Phys. 2016 Mar;43(3):1369-73. doi: 10.1118/1.4942381. PMID: 26936721

Feasibility evaluation of diffusion-weighted imaging using an integrated MRI-radiotherapy system for response assessment to neoadjuvant therapy in rectal cancer. Shaverdian N, Yang Y, Hu P, Hart S, Sheng K, Lamb J, Cao M, Agazaryan N, Thomas D, Steinberg M, Low DA, Lee P. Br J Radiol. 2017 Mar;90(1071):20160739. doi: 10.1259/bjr.20160739. Epub 2017 Jan 12. -4 Many of our users have reported that on-table adaptive replanning takes on average an additional 15 minutes. Approximately 10 minutes of this time is due to the contouring constraint "hurtle" [sic] ? turtle? We believe that improvements in computational speed and algorithms under development will speed up the turtle. Edit: remove bold

Can you describe/explain the technical differences between the MRIdian linac compared to a regular linac (i.e., type of waveguide, are there flattening filters, differences in the MLC, bending magnetic, magnetron, accelerator tube)?

spald01

There's no difference, we just have shielding technologies that allow a conventional Linac to operate next to the MRI.

What was it like making the jump from academia to the start-up world? DId you handle the business aspects or did you partner with someone?

nate

I have always partnered with a team of people. "If you have a dream and you want it to come true, you have to share the dream"

Thanks for coming to talk with us! My father-in-law had side effects from radiation therapy for prostate cancer that diminished his quality of life. Has there been any progress in treatment for prostate cancer that lowers the risk of side effects?

asbruckman

We believe technical innovations in optimizing dose and image guidance have the potential to spare organs nearby the prostate from the risk of radiation damage. Having MR imaging available on the treatment system allows the physician to see the prostate, rectum and the bladder before therapy, on-table to re-optimize the radiation plan if necessary. During treatment the system continually images the tissues to stay on target.

What are Viewray's plans to compete for market share with the Elekta Unity coming online at Utrecht, MD Anderson, and several other major cancer centers right now? How would you compare the systems and what are MRIdian Linac's advantages and disadvantages to Unity?

spald01

At ViewRay we design systems that are capable of obtaining FDA and CE mark clearances. We've been treating cancer patients since 2014 with diagnostic quality MRI, on-table adaptive planning and soft tissue tracking. We have 8 first generation systems and 3 second generation Linac systems installed. In July 2017 Henry Ford Health Systems began patient treatments with the MR-Linac system. By being the first to deliver a system to treat patients with unparalleled features and performing clinical studies to demonstrate value we believe we will remain the market leader.

Does the magnetic field affect the dose distribution in patients in regards to the production of free radicals in the tissue?

rysvel

The polarization of atoms and particles by the magnetic field in MRI is actually very weak. At 0.35 Tesla approximately 1 part per million of the hydrogen nuclei are polarized in alignment with the magnetic field. This is a competition between the Zeeman effect and thermally induced molecular collisions. While polarized atoms and particles could change the interaction probabilities and hence the production of free radicals, the very weak polarization makes it negligible.

Hi Dr. Dempsey, I'm in school to get into this field, and have been doing some reading on this subject. I have some questions, but also feel free to set straight any faulty assumptions that might be guiding these questions.

1. Why .35T specifically? I understand lower field strength means smaller the susceptibility artifacts,

but how did your group decide on that strength? Have you considered increasing your magnet strength down the road?

2. How close are we to wide scale application of ART with Meridian? I have seen that it has been done, but am curious about QA and how comfortable physicians are handing control over to an algorithm.

3. I've been thinking about the future of this technology and would like to hear your thoughts about where we are going. A lot of cancer therapy has been pushing towards hypofractionation and moving from Co-60 to a linac helps with that, but what are the next steps?

KrimsonKing

1- The main driver was to not distort or trap dose by higher magnetic fields. Detailed physics modeling identified 0.35 T as the optimal field strength. The lower field strength also makes the chemical shift, susceptibility distortions, and SAR insignificant.
So no desire to raise the field strength, with our breakthroughs in fast imaging that are under development and an unwillingness to compromise dosimetric quality we do not see any advantage to doing this. 2- All MRIdian and MRIdian MR-Linac user have a clinical system that supports on-table adaptive. The physicians do not "hand over control to an algorithm". The physicians control the process and the quality of the plans using very fast contouring, dose computation, and optimization tools, very much like other systems, just a lot faster. A secondary independent Monte Carlo model acts as a check for on-table IMRT QA. 3- We agree that hypofractionated MRI-guided radiation therapy has great potential value and we are testing this by supporting prospective clinical trials.

Could this new technology be used with proton therapy and do you think it would be more effective in treating brain tumors?

kiki964

Not off the shelf, but we'll look into it. Our clinical collaborators are very excited about the potential of the MRIdian MR-Linac to treat brain tumors.

Thanks, very kind of The Winnower.

What do you think the ultimate potential of deep learning networks is for identifying cancer cells, and what do you think of the technology more generally?

01-MACHINE_GOD-10

This is more of a diagnostic application, we are a company focused on cancer treatment. It's an interesting application, we wish them success but this is outside the scope of our work.

Can you describe the difference between the MRIdian Co-60 system to the MRIdian Linac System?

1) What sort of things did you have to modify in the MRIdian co-60 system to enable the MR component for the MRIdian Linac?

2) What did Viewray choose a 0.35T field strenght

3) What type of algorithm is used for Viewray's treatment planning software?

spald01

1 - Only the radiation delivery system was modified. 2 - It's the best trade-off between MRI diagnostic quality and unperturbed dose distributions. 3 - Monte Carlo simulation.

As a nuclear Chemist, do you feel like you have been exposed to radiation at dangerous levels or just exposed to it more than an average person? Will there be further advancements that you already know of as of now in the radiation treatment strategies as a method of killing off cancer cell? Thanks

godofwar5151

Radiation exposure risks are now well understood, and the policies and procedures for safely working with radiation are well developed. Therefore, I do not feel that I'm taking any significant risks. On the second question - Yes, we're working on that.

What are the biggest problems you encounter when using radiation for testing?

Harryrsims

It's not really a problem, but it requires a lot of work to perform radiation testing. When using radiation for testing, we must use phantoms, i.e. blocks of plastic or tanks of water, to interact with the radiation beam so we can test our models of radiation transport and dose deposition. Obviously, we can't test on human beings because the exposure risk is not justified. The test methods and standards for creating safe and effective radiation systems are well developed and we design our systems to pass all those tests.

How does the vray system compare to the elekta system?

Mooserthedog

This is a little difficult for us to say as the Elekta system appears to still be under development. We should not make comparisons until they are clinical. A press release from Nov. 10th 2017 states:"Elekta CEO, Richard Hausmann, comments: “Although development and final testing of Unity is progressing well, I decided to take a bit more time because I want to be certain that the high field strength of our solution can be optimally used from the first release... "

https://www.elekta.com/meta/press-all.html?id=1390096

What are your thoughts on Dr Burzynski's successful treatments of cancers with antineoplastons ?

Truthplease5

I would refer you to the NCI page