POINT/COUNTERPOINT

Suggestions for topics suitable for these Point/Counterpoint debates should be addressed to Colin G. Orton, Professor Emeritus, Wayne State University, Detroit: ortonc@comcast.net. Persons participating in Point/Counterpoint discussions are selected for their knowledge and communicative skill. Their positions for or against a proposition may or may not reflect their personal opinions or the positions of their employers.

Data-driven motion correction will replace motion-tracking devices in molecular imaging-guided radiation therapy treatment planning

Adam Kesner, Ph.D.
Department of Medical Physics, Memorial Sloan Kettering Cancer Center, New York, NY, USA
(Tel: 212-639-6371; E-mail: kesnera@mskcc.org)

Tinsu Pan, Ph.D.
Department of Imaging Physics, The University of Texas, M D Anderson Cancer Center, 1515 Holcombe Blvd., Unit 1352, Houston, TX 77030-4009, USA
(Tel: 713-563-2714; E-mail: tpan@mdanderson.org)

Habib Zaidi, Ph.D., Moderator

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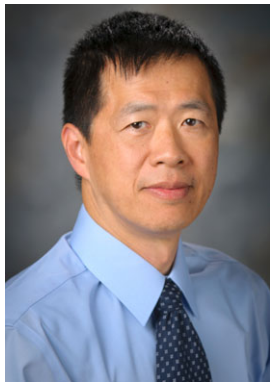
OVERVIEW

The last decade has seen abundant literature demonstrating the advantages of hybrid-imaging modalities combining morphological and molecular imaging in clinical oncology. Commercial systems merging SPECT and CT, PET and CT, or PET and MRI are now widely used in the clinic and have had significant impact on patient management. Ultimately, molecular imaging-guided radiotherapy holds the promise of improved definition of tumor target volumes. However, respiratory motion management remains one of the main challenges of this technique. This has historically been handled using motion-tracking devices (MTDs), but recent advances enable one to obtain motion information from the acquired image data, thus allowing the implementation of data-driven motion correction (DMC) strategies. MTD use signals from optical or mechanical surrogates, for example, Varian RPM or bellows, which are temporally synchronized with CT or PET signal acquisition. DMC uses signals extracted from the imaging data itself to track the respiration phase or displacement during the acquisition of the raw imaging data. While some think that novel data-driven motion correction is robust enough for clinical adoption in the context of molecular imaging-guided radiation therapy, others think that these techniques do not constitute a viable solution and that conventional motion tracking devices are still required and that the time when they should be abandoned did not come yet. This is the topic of this month's Point/Counterpoint debate.

Arguing for the Proposition is Adam Kesner, Ph.D. Dr. Kesner received his Ph.D. in Biomedical Physics from the University of California, Los Angeles, USA, in 2008. On graduation, he assumed a position supporting medical physics global health initiatives at the IAEA in Vienna, Austria.

In 2011, Dr. Kesner received US Fulbright and Golda Meir awards for a postdoctoral fellowship at the Hebrew University in Jerusalem, Israel. On completion, Dr. Kesner earned ABR certification in Nuclear Medical Physics and joined the faculty at the University of Colorado, before ultimately joining the faculty at Memorial Sloan Kettering Cancer Center, New York, USA, in 2017, in his present position as assistant attending physicist. Dr. Kesner has made original contributions in the subfield of data-driven motion management in nuclear imaging, pioneering the foundational concepts that motion information can be revealed in signal fluctuations, PET can be reconceived as an inherent motion-capturing modality as well as data management strategies for fast, real-time capable processing.



Arguing against the Proposition is Tinsu Pan, Ph.D. Dr. Pan is a professor in the Imaging Physics and Radiation Physics Departments of the University of Texas, M.D. Anderson Cancer Center. He received his postdoctoral training in Nuclear Medicine under Dr. Michael A. King in the University of Massachusetts Medical Center from 1992 to 1996. He was a senior scientist in the Applied Science

Laboratory of GE Healthcare where he designed the cardiac CT and invented 4D CT on the GE CT scanners from 1996 to 2003. He joined the M.D. Anderson Cancer Center and invented average CT to improve the alignment of PET and CT on the GE PET/CT scanners in 2004. Average CT has been gaining popularity in RT dose calculation and IGRT. His research interest is in the thoracic imaging with CT and PET/CT. Dr. Pan is certified by the ABR and ABSNM. He has more than 10 patents, 10 book chapters, and 120 publications.

FOR THE PROPOSITION: Adam Kesner, Ph.D.

Opening Statement

Data-driven motion correction represents a shift in our understanding of imaging technology — we are seeing that our systems are collecting more robust information than we have traditionally considered. A growing number of research studies have demonstrated that we can extract motion-related information from our raw image data. DMC strategies have been presented for PET,[1] CT,[2] and MR.[3] These new tools expand our capacity to address issues stemming from patient motion. This innovation may be of particular relevance for target delineation in radiotherapy treatment planning, which can benefit from improved motion management techniques and strategies.

While DMC methods vary, they are generally built around the concept that raw image data contains information about the temporal and spatial coordinates of the signal they represent. Fluctuation patterns in these signals can provide a characterization of patient motion. This characterization is analogous to, and can replace, signals from MTDs used with traditional hardware-driven motion correction. In PET imaging, studies have shown that DMC- and hardware-driven strategies can provide similar image quality.[1] However, DMC may offer practical advantages: it can be implemented with no extra effort on the part of the camera operators, provide standardized performance, and will not impose changes to traditional PET image acquisition protocols. Because of the potential for full automation of DMC implementation, it can be envisioned that these methods may support a PET field where the integration of motion management becomes routine with all acquisitions.[4]

Radiotherapy treatment planning represents a key area that may be impacted by improvements in and standardization of 4D PET. It is already common for treatments to integrate motion information via gated or motion-corrected delivery regimens based on 4D CT-derived treatment planning.[5] It is also common for PET to be incorporated with planning procedures for treatments of many sites including lung.[6] While the integration of PET with treatment planning is used in many radiotherapy centers, 4D PET is less prevalent, yet it has been shown to provide value.[7] As the principles of 4D treatment planning are already well established, it is likely that easily accessible 4D CT and 4D PET images acquired through DMC methods will readily integrate into clinical procedures and support improved delineation of anatomical and functional targets. Improved delineation via the application of DMC may also support treatment strategies like hypofractionation and stereotactic body radiation therapy, which rely on reduced margins to minimize the dose to normal tissue.[8] In addition, DMC is inherently driven by the detection of internal motion rather than surrogate measures, and this may provide further advantages over current technologies.

At present, no DMC PET products are commercially available. However, once the technology completes its transition from academia to industry, it is reasonable to think that it may lead to a new standard of care in motion-managed radiotherapy treatment.

AGAINST THE PROPOSITION: Tinsu Pan, Ph.D.

Opening Statement

Data-driven motion correction for PET image reconstruction is a technique that corrects PET images degraded by respiratory motion using the motion information extracted directly from the PET data without any MTD.[9] With improvements in sensitivity and computing hardware on the modern PET/CT scanners, it is expected that PET/CT scanning of today will become DMC PET/CT imaging of tomorrow with a similar acquisition time. However, DMC PET/CT will not void the need of MTD for PET/CT-guided radiation therapy planning (RTP) because it will be a part of PET/CT-guided RTP, and it will need MTD-driven 4D CT to be compatible with current RTP processes.

Both 4D CT and 4D PET were developed in 2002.[10,11] Today 4D CT is a standard clinical procedure in RTP, yet 4D PET is still in research. One possible explanation is that the use of MTD makes 4D PET not acceptable for clinical radiation therapy use. If the suggestion is true, then 4D CT should not have been successful in RTP because almost all 4D CTs are equipped with MTD except for one recently developed data-driven 4D CT.[2] 4D CT provides the tumor motion information critical for treatment planning. Without that, it will be difficult to determine the extent of tumor motion. The recent success of stereotactic body radiation therapy in treating early-stage lung cancer is due, in part, to the availability of tumor motion information from 4D CT.[12] Clinical evidence of 4D CT to improve RTP is readily available. There is little clinical evidence that 4D PET improves tumor detection, staging, or RTP. 4D CT should be an integral part of PET/CT or 4D PET/CT for RTP because it provides the maximum intensity projection (MIP) images for depicting the region containing the tumor motion trajectory and for limiting the PET functional activity to this region. In addition, the average intensity projection (AIP) images derived from 4D CT are needed for PET attenuation correction,[13] RT dose calculation,[14] and image-guided RT.[15] 4D CT can also help quantification of 4D PET data. Visualizing the patient's MTD respiratory traces over multiple

breathing cycles provides the opportunity to assess 4D CT quality, to mitigate the impact of irregular respiration in 4D CT prospectively,[16] or to plan gated treatment with breath-hold. MTD will always be needed for PET/CT-based RTP and for motion-synchronized treatment delivery even though DMC PET/CT may not need it.

Reimbursement of only one PET scan before cancer treatment also limits the application of 4D PET in RTP because most patients utilize their PET scan for their initial clinical evaluation. Currently, integrating molecular imaging into RTP involves registering a treatment-position simulation CT with a diagnostic PET/CT rather than a simulation PET/CT, which requires longer patient setup and acquisition times if 4D PET is to be used. The newer high sensitivity PET/CT scanners and advanced reconstruction strategies of combining all phases of PET data into a single motion-corrected PET image could potentially make 4D PET more clinically acceptable if the workflow can be streamlined and the scan time shortened further. To embrace the future of DMC PET in RTP, one has to address the clinical efficacy of 4D PET. Is 4D PET indispensable like 4D CT in the context of RTP?

Rebuttal: Adam Kesner, Ph.D.

I agree with my opponent on the point that DMC 4D PET will likely not displace MTD-driven 4D CT; however, I submit that the two technologies are not incompatible with each other. On the contrary, I believe that their overlap will be the winning path to acceptance of 4D PET in RTP.

Four-dimensional PET is to 3D PET as 4D CT is to 3D CT — an expansion of the modality to map signal over the motion cycle. The role of anatomical imaging has always had clear utility in RTP, and the acceptance of 4D CT in RTP has progressed in part due to its obvious benefit. The role of functional imaging in RTP has been a supplementary one: PET and the functional information it provides can enhance anatomy-based RTP. 4D PET has a promising role in RTP[17,18] but does not currently have an obvious or "indispensable" benefit. However, the associated cost–benefit consideration of 4D PET technology is made more favorable by the convenience offered by DMC strategies, which can bring the cost of acquisition, in terms of added effort, virtually to nil. That practical advantage is why DMC stands out as a transformative technology that will replace MTDs in molecular imaging-guided RTP.

In summary, 4D PET is not new, it is not indispensable, and its utility in RTP remains unestablished. However, we have seen significant interest for integrating motion-corrected PET in RTP coupled with repeated calls for innovation in the technology to make it more practical in the radiotherapy clinic[17–19]; DMC methods are an answer to these calls. The value of DMC PET will be in the practical attributes associated with its implementation: easy generation of 4D PET images, standardized performance that can support standardized processing protocols, and ubiquitous generation of motion-corrected PET images. Research will likely resurge in this area with a new capacity to generate large population validation studies with relative ease. These studies will help 4D PET fulfill its potential and provide appropriate justification for new clinical standards and reimbursements.

Rebuttal: Tinsu Pan, Ph.D.

I share the enthusiasm of my opponent on the use of DMC PET for improving PET image quality. However, in the application of PET/CT for RTP, use of MTD will still play an important role even though DMC PET does not need an MTD. There are still challenges in 4D PET today for DMC PET to overcome in the future: (a) long acquisition time, (b) complex processing procedure, (c) patient selection as to which patients are going to benefit from 4D PET and how to triage the patients without their prior images. Integration of DMC PET and 4D CT is necessary and important when DMC PET is to be used in RTP. It is not clear if 4D CT will be one day without MTD as MTD currently provides the important functions of assessing reproducibility of the respiratory motion in 4D CT and assessing suitability of a breath-hold patient for RT. Finally, the clinical value of 4D PET over PET with and without 4D CT in RTP needs to be demonstrated for the future success of DMC PET for RTP.

CONFLICTS OF INTEREST

Dr. Kesner and Dr. Pan have no relevant conflicts of interest.

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