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Commercially competitive vendor-agnostic image reconstruction could be a leap forward for PET harmonization

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Author:

Adam L Kesner, PhD, DABR

Associate Attending, Nuclear Imaging Physics

Department of Medical Physics

Memorial Sloan Kettering Cancer Center

1250 First Avenue, Room S-1119E (Box 84), New York, NY 10065

T 212-639-6371 F 212-717-3010

kesnera@mskcc.org

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Dear Dr. Czernin,

I read with interest the recent publication in JNM titled "A guide to ComBat harmonization of imaging biomarkers in multicenter studies" (*1*). The work discussed in the article presents valuable ideas and concepts to the community and continues a tradition of inspired diligence that has ushered our field towards an increasingly efficacious infrastructure for PET harmonization. Efforts to improve harmonization in PET metrology provide a significant and fundamental contribution to the field because they support our ability to work confidently with images and develop meaningful clinical assessments and innovations.

Image reconstruction is a central step in the image generation process. In recent years, significant gains have been made in PET image quality at the stage of image reconstruction, we can note that application of the technology has transitioned into the proprietary and vendor-specific domain. As we look to the future and see inevitable evolution of artificial intelligence aided reconstruction, we can expect that in the coming years it will likely be more difficult to fully describe reconstruction algorithms because they will be partially defined by the select training data sets used to build them (*2*). It appears that we are on a trajectory that will usher in continued divergence of advanced reconstruction algorithms across vendors, increased layers of vendor specificity, and subsequently greater challenges to harmonize PET.

The field of data science is continually maturing, perhaps most notably in the areas of artificial intelligence and radiomics. Simultaneously we are learning to take on new roles as stewards of data(*2,3*). Our growth in this realm is relevant for harmonization efforts because the prospect of evolving the field towards greater access to raw data has many implications, including the potential to create reliable, cross-platform image reconstruction tools. Such a solution could present an ideal, alternative strategy for addressing the "scanner affect", essentially through reducing the (technically unnecessary) variability of vendor-specific image reconstruction algorithms across scanners.

The importance of homogenizing PET data is fundamental to the field. A basis for the advancement of diagnostic imaging are standards established through multicenter trials. The greater the uncertainty in the trial data, the greater the possibility a study will be underpowered, and it adds an increased possibility of the trial producing incorrect conclusions (*4*). Uncertainty stems in part from variability in the image generation processes and can be addressed through standardization and/or harmonization. We can recall *standardization* refers to the process of making something conform to a standard whereas *harmonization* is the action, or process, of making something consistent or compatible. The former is

preferable where possible – we cannot reasonably standardize hardware, but we could create the means to standardize processing, in support of those applications of PET that can benefit from it. A recent review of multicenter use of PET/CT concluded that "standardization" of acquisition and processing "should precede any multicenter trial that uses PET SUVs quantitatively"; and that "This should be a high priority for future multicenter trials using quantitative imaging." (*5*). The priority is echoed and amplified if we consider the field's collective responsibility to ensure that our patient's data is being used for optimal benefit (*3*). It therefore becomes prudent to recognize that an infrastructure that supports optional standardized advanced image reconstruction is preferential.

We are at least several years away from having reliable third party PET image reconstruction tools – it is possible from a technical standpoint, but we do not presently have the industrial framework to support it, and raw data formats as well as reconstruction algorithms are proprietary. But whether we are several years away from realizing this solution, or several decades, may depend on if we are willing to have the requisite discussion now. Several pathways could be considered for implementation. One method could be tuning PET systems to produce reliable, compliant raw data formats, which could enable investment in creating competitive cross-platform processing tools.

Data access across imaging is in fact large and consequential topic. Harmonization in PET is one of many topics that are connected to this faucet on our infrastructure. Generally, access to data for third party solution development addresses a central pivot of the PET instrumentation field and would have wide ranging implications for innovation beyond, and downstream of, improved harmonization and/or standardization (*6*). Radiomics, AI, and other avenues of imaging data science would directly reap the benefits – access to data and its quality (fidelity) is a new bottleneck for technological advancement. Although the topic of data access is complex, cross-vendor reconstruction for supporting harmonization efforts would be a straightforward and logical solution for addressing the harmonization problem at its crux. Correspondingly, the clear and concise implication of unified reconstruction in the harmonization challenge lends support to the more general assertion that greater access to data should support a more efficacious modern imaging field.

In summary, practical solutions, such as those presented by the authors, provide real benefit to the field. But as we look to the future, it is time to add agnostic image reconstruction to the discussion of solutions for harmonization. The same advancements in computing technology that have enabled new advances in image reconstruction make it prudent to reevaluate our infrastructure for accessing and using data at its source.

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