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Reply:

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REPLY:

We appreciate the comments by Dr Giannelli and colleagues regarding our recent article "Treatment Response Prediction of Nasopharyngeal Carcinoma Based on Histogram Analysis of Diffusional Kurtosis Imaging," which raised an interesting issue on the influence factors of diffusional kurtosis imaging (DKI) estimation bias.

As they mentioned, DWI with 3 diffusion-weighted directions is currently the de facto standard in the application of DKI in body tumor. There are objective reasons for using 3 perpendicular directions in body application of non-Gaussian diffusional kurtosis imaging rather than >15 directions as in brain white matter evaluations.[1] First, the different anisotropic features between body and head lead to a basic need for >15 directions in white matter applications, while 3 directions may be sufficient in body applications.[2] Second, the increase of directions will result in a large increase in acquisition time, more likely leading to bulk and respiration motion, which should be avoided in body imaging acquisitions. Third, trace weighted images (TWIs) could increase the low signal-to-noise ratio in body tissue and make images robust to motion.[3,4]

Giannelli et al have reported that the percentage error in K and D estimation using TWIs in head and neck cancer can be non-negligible for single lesions. They recommended the use of at least 15 diffusion-weighting directions and 2 non-null b-values in quantitative DKI analysis based on a simulation study[5] and a prospective study.[6] They drew this conclusion on the basis of a small sample study with a group of 18 patients with significantly different types of head and neck tumors, for example, tongue squamous cell carcinoma and lymphoma, using 3 main diffusion directions (x, y, z) with an acquisition time of 8 minutes 21 seconds (the time of our study is 3 minutes 26 seconds).

As we all know, different types of tumors have remarkably different biologic microstructures, resulting in differing diffusivity. For example, nasopharyngeal carcinoma (NPC) is a special type of head and neck tumor that has remarkably different biologic characteristics than other head and neck tumors. It is relatively isotropic, though the microstructure complexity differs according to treatment response.[7] Moreover, the acquisition of NPC MR images is relatively more sensitive to bulk and respiratory artifacts; therefore, an appropriate short acquisition time is important. Therefore, the reproductivity and reliability of the recommendation for more directions not only in patients with NPC but also in those with other head and neck tumors remains controversial and needs further validation in unique types of tumors with certain sample sizes. Moreover, it appears that the DKI parameters may differ among different MR imaging systems and different institutions.[8-10] Further study should be a multicenter large-sample-size prospective validation of this recommendation. The more complex the algorithm, the more error will occur during each step of calculation. Hence, a simplified geometric model may be more feasible in clinical application.[11]

In conclusion, the use of only 3 perpendicular directions in general DKI body applications may lead to non-negligible bias during calculation. However, in body solid tumors with fewer anisotropic characteristics, 3 directions may be sufficient in clinical application. These comments remind us to pay more attention to the influencing factors of DKI acquisitions. On the other hand, because the imaging biomarkers differ in numerous studies,[7,8,10,12-14] these comments give us an idea of how to explain the variation among these studies, to modify the parameter calculations, and to increase the possibility of exploring unique, proper, and impactful metrics as image biomarkers for further clinical application.

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