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In Regard to Yang et al

To the Editor: The article by Yang et al (1) describes an interesting approach for markerless lung tumor detection and tracking in cone beam computed tomography (CBCT) projections, using prior CT information to remove overlying anatomy signals. The proposed method is strikingly similar to the CT-based contrast-enhancement technique that we described previously (2), although some differences are evident. The authors obtain the “anatomy-without-tumor” dataset from the CT volume by masking the tumor with the average lung tissue value. We proposed the masking not only of the lesion but of the whole lung region, because simply masking the tumor was proved to lead to higher tracking sensitivity to tumor position on CT scans. In addition, the rigid registration described by the authors between CBCT projections and “anatomy-without-tumor” digitally reconstructed radiographs may not take into account nonrigid mismatches of the anatomic structures. Our approach was based on deformable registration between the “anatomy-without-tumor” dataset and the reconstructed CBCT volume, before generating digitally reconstructed radiographs. Finally, we proposed to derive the “tumor-only” templates for cross-correlation from a single 4-dimensional (4D) CT phase. Conversely, Yang et al used the “average CT” dataset, which may not reflect the lesion’s size and shape in CBCT projections.

In light of these considerations, we were highly surprised by the fact that Yang et al reported lung tumor position detection capability on every CBCT projection obtained with $\pm 180^\circ$ angular range. According to our experience (2), testing on CBCT projections coming from the same Elekta Synergy machine on lung cancer patients treated by stereotactic body radiation therapy revealed that, especially on projections close to the latero-lateral direction, the overlap of the surrounding anatomic structures completely hindered lesion visibility, thus excluding any detection possibility both with conventional and contrast-enhancement methods. A comparison between the detection capability of the proposed markerless technique and the state-of-the-art algorithm, based on templates generated from planning 4D CT images (3), would have allowed an objective assessment of the effective gain of the described technique on the specific 4-patient dataset used for testing.

Our final remark concerns the way in which the target tracking accuracy was measured. Yang et al compared the supero-inferior distance between the average tumor positions identified on CBCT images and the projected isocenter with the supero-inferior distance between the 3-dimensional (3D)/4D CBCT average tumor position and the 3D isocenter. We believe that tracking accuracy should be investigated along the 3 main anatomic axes, by directly comparing the reference 3D lesion coordinates extracted from 3D/4D CBCT and the 3D tumor coordinates reconstructed from the detected positions on CBCT projections.

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In Reply to Fassi et al

To the Editor: We welcome the authors’ comments on our recently published manuscript (1, 2). We acknowledge the similarities with the authors’ work (3), which, as an abstract, was neither known nor available to us at the time of submission.

In their letter, the authors express 2 main concerns, which we address in turn. First, we used the “average CT” dataset to generate digitally restored radiographs (DRRs) for subsequent tumor removal from kV images, whereas the abstract authors used a single phase from a 4-dimensional computed tomography (4DCT) dataset. Although we appreciate that there are subtle differences between the 2 methods, we do not believe that this would adversely affect our results. A contour on an average CT will necessarily include the tumor in all phases of a 4DCT. This results in removal of a larger volume, but does not affect tumor detection. A further benefit of using the average CT dataset is that we can use the actual clinical contours rather than generating a new set of contours on a single 4DCT phase.

Second, the authors raise a concern regarding detection capability. We agree that, at some angles, the over- and underlying structures make detection challenging, and our methodology was

optimized to address this. Details were admittedly sparse because of word limits imposed by this journal. Briefly, during the registration of the DRR of anatomy-without-tumor to the projections, a region surrounding the tumor location is excluded. The size of the region of interest for anatomy-without-tumor is optimized to achieve the best matching and subtraction results. For the evaluation of detection accuracy, we had long discussion with the reviewers of our paper. We used an anatomical phantom for the initial evaluation, and the detected tumor positions match very well with 1-dimensional motion. In the evaluation of patient data, individual projections contain only 2-dimensional information with the direction perpendicular to the longitudinal direction changing continuously during gantry rotation. For this reason, we evaluated only the motion in the longitudinal direction by comparing with average tumor positions. More fundamentally, we do not have a ground truth of tumor positions for patient studies. It is difficult to locate lung tumors manually on all projections (4), as the tumors are simply not visible at some projection angles.

In conclusion, we understand that our accuracy evaluation remains somewhat incomplete. We are presently constructing a sophisticated respiratory torso phantom that will have all organs to move and deform in 3 dimensions in a reproducible manner.

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In Reply to Zagar and Marks

To the Editor: We appreciate the excellent comments from Drs Zagar and Marks (1) regarding esophagus delineation of our atlas (2). Contouring esophagus without oral contrast can be challenging. We agree that the esophagus is often tortuous and can be

difficult to identify. We also agree that diluted oral contrast can be useful for delineating esophagus. Coauthors of this atlas have different opinions on this: some agree with you, while others retain concerns.

Of note, presence of contrast may change shape and volume of the esophagus in a dosimetrically significant way (Fig. 1). In this case, the esophagus delineated with dilute oral contrast (red) appears to be less tortuous and longer inferiorly than the esophagus without contrast (green). The volume of the esophagus was larger with contrast. Enlarging the esophagus or changing the shape of the esophagus may artificially lower the mean doses or alter the estimation of maximum esophageal dose depending on the relative location of the tumor and esophagus. This can be remarkable when a highly conformal plan with sharp dose fall-off is designed or when dose prescription is strictly limited by the maximum and mean esophageal doses such as in the Radiation Therapy Oncology Group 1106 protocol.

There are other factors to contemplate when considering oral contrast, for example, (1) swallowing effort may cause the patient to shift position; (2) swallowing action may change breathing patterns, impacting motion assessment during 4-dimensional computed tomography; (3) placing oral contrast is challenging in patients who require simulation with active breathing control which requires a mouthpiece; and (4) the amount of contrast may vary in parts of the esophagus and from patient-to-patient due to complexity of contrast administration.

Overall, we appreciate the valuable comments but cannot agree that increased accuracy with contrast outweighs potential anatomy distortion. More accurate contouring may not necessarily equate with better simulation of the treatment situation. Before outcome data become available, we recommend that readers individualize use of oral contrast. When it is deemed essential, (eg, when tumor and esophagus are adjacent), contrast should be diluted, amounts should be controlled, and a standard procedure should be followed to minimize changes in volume and shapes and thus ensure reproducibility. Further study with a large number of cases with correlation to clinical esophagitis is needed before a more definitive recommendation can be made. Should you and Drs Zagar and Marks have further questions regarding this, please feel free to contact us.

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