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Human Cerenkov Imaging Using ^{18}F-FDG

TO THE EDITOR: We read with great interest the ahead-of-print article of Thorek et al. (*1*) recently published online in *The Journal of Nuclear Medicine* on human Cerenkov imaging using ^{18}F-FDG. Having obtained a similar finding (*2*) using ^{131}I, we would like to share our knowledge on this topic and comment on some specific claims.

The first issue we would like to underline is related to the set-up of the imaging apparatus. More precisely, it is well known that the Cerenkov light spectrum has an inverse square dependence on the wavelength (*3*) and, thus, is more intense in the ultraviolet region than in the visible region. However, if one considers the strong tissue absorption of light below 620 nm caused by hemoglobin, the spectrum of the Cerenkov radiation escaping from the tissues contains mainly wavelengths above 630 nm. In a recent paper (*4*), cited also by Thorek et al., we showed that to improve the in vivo detection of Cerenkov sources it is useful to optimize the optical imaging system in the red, near-infrared region (650–850 nm). It is thus not clear to us why the authors decided to use a short-pass filter with a cutoff at 605 nm since in this way they rejected most of the Cerenkov light reaching the body surface. We also are interested in knowing the characteristics and the manufacturer of the objective used to acquire axilla images (estimated field of view, at least 10 × 10 cm) at a very short distance.

Looking at Figure 2, we noticed the absence of any direct charge-coupled-device detection of γ rays. This is a bit surprising considering also the small working distance from the patient (8 cm). It would thus be interesting to know if the authors applied any γ-rejection algorithm.

Thorek et al. (*1*) claimed that our human Cerenkography image was obtained with a much higher dose of ^{131}I. This is not entirely true, since the difference between the injected doses is only 14%, or more precisely, 550 MBq of ^{131}I with respect to 470 MBq of ^{18}F-FDG for the representative patient shown in Figure 2. Second, for a fair comparison of the results in terms of Cerenkov light production, it is useful to remember that the emission of Cerenkov radiation is closely related to the decay scheme of the radioisotope; in this case, ^{18}F emits about 2.5 times more Cerenkov light for each decay than does ^{131}I (*5*). We do agree that ^{131}I thyroid uptake can be typically up to 50%, resulting in an equivalent ^{18}F-FDG uptake of 110 MBq. Considering a spheric lymph node 1.5–2 cm in radius and an uptake value of 0.05 MBq/mL, the corresponding ^{18}F-FDG activity is approximately 0.7–1.7 MBq—that is, 2, not 4 (!), orders of magnitude less than the value claimed in the "Discussion" section by Thorek et al.

Figure 3 of the article by Thorek et al. (*1*) plots a correlation between the Cerenkov signal and the ^{18}F-FDG concentration measured by PET. This correlation measured in vivo is somewhat surprising since, in this case, the different tissue attenuation (e.g., >different source depth) and not the source strength (MBq/mL) should dominate in determining the average value of the detected Cerenkov signal. Also, the plotted data show that the magnitude of the Cerenkov signal is almost comparable to the contralateral side (except for a single patient). In particular, by considering the point corresponding to the patient in Figure 2 (maximum ^{18}F-FDG concentration. 0.05 MBq/mL), one finds a small difference with respect to the contralateral side points.

Thorek et al. (*1*) provides a set of system linearity measurements by performing in vitro imaging of a 24-well polycarbonate plate filled with ^{18}F-FDG at different time points and, thus, of different concentrations. As one can see by looking at Figure 1A of the article, the detected Cerenkov signal is quite noisy at a concentration of 0.1 MBq/mL even without any attenuating material. We were thus a bit surprised that the authors were able to detect, at a tissue depth greater than 1 cm, a Cerenkov signal corresponding to an ^{18}F-FDG concentration of 0.03–0.05 MBq/mL. Figure 2 also seems to show that the patient was not shaved, thus making it even more surprising that the authors could detect Cerenkov light crossing the axillary hair.

To summarize, the paper of Thorek et al. (*1*) contains some puzzling imaging methods and results that in our opinion need to be better explained or justified.

Note: The ahead-of-print article (*1*) of Thorek et al. was modified after the submission of our letter to the editor. Our criticisms related to the optical filter and the correlation shown in Figure 3 no longer apply to the final version (*6*).

REFERENCES

1. Thorek DL, Riedl CC, Grimm J. Clinical Cerenkov luminescence imaging of ^{18}F-FDG. *J Nucl Med.* September 27, 2013 [Epub ahead of print].
2. Spinelli AE, Ferdeghini M, Cavedon C, et al. First human Cerenkography [letter]. *J Biomed Opt.* 2013;18:20502.
3. Jelley JV. *Cerenkov Radiation and Its Applications.* London, U.K.: Pergamon; 1958.
4. Spinelli AE, Boschi F. Optimizing in vivo small animal Cerenkov luminescence imaging [letter]. *J Biomed Opt.* 2012;17:040506.
5. Liu H, Ren G, Miao Z, et al. Molecular optical imaging with radioactive probes. *PLoS ONE.* 2010;5:e9470.
6. Thorek DL, Riedl CC, Grimm J. Clinical Cerenkov luminescence imaging of ^{18}F-FDG. *J Nucl Med.* 2014;55:95–98.

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