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# Off-Target Report on $^{18}$F-Sodium Fluoride PET/CT for Detection of Skeletal Metastases in Prostate Cancer

To the Editor:

In a recent report in the *Journal of Nuclear Medicine*, cited by AuntMinnie, Zacho et al. found according to the title of their communication "No added value of $^{18}$F-sodium fluoride PET/CT for the detection of bone metastases in patients with newly diagnosed prostate cancer with normal bone scintigraphy" (*1*). In 81 intermediate- or high-risk prostate cancer patients with negative bone scintigraphy scheduled for prostatectomy, NaF-PET/CT "indicated bone metastasis" in one and was equivocal in seven patients, and none of these patients exhibited biochemical failure (PSA level ≥ 2 ng/mL six weeks/six months after radical prostatectomy), whereas all six patients with biochemical failure had negative NaF-PET/CT (and negative bone scintigraphy) – findings making the authors conclude as stated in their title.

Their report is off-target because: 1) skeletal metastases are bone *marrow* and not bone metastases and 2) neither NaF-PET/CT nor bone scintigraphy mirror bone marrow metastases, but late occurring bone changes that may or may not be due to active cancerous processes (*2,3*). As in other recent communications (*4,5*), the authors disregarded the true nature of skeletal metastases, which home and grow in the bone marrow long before they give rise to structural changes in the osseous bone substance that can be detected by bone scintigraphy, NaF-PET/CT or other imaging modalities. This was highlighted more than 10 years ago by Basu, Alavi et al. (*6,7*) and has recently given rise to comments in both *Journal of Nuclear Medicine* and *European Journal of Nuclear Medicine and Molecular Imaging* (*2,3*), the latter calling for a much needed paradigm shift, since we cannot go on using

methods unable to fulfil their stated purpose and which, therefore, unfortunately, may lead to inappropriate patient management.

The reason why Zacho et al. didn't observe an association between biochemical failure and abnormal NaF-PET/CT findings is a simple one: there shouldn't be an association – at least not a very close one. An increase in PSA, however unspecific, is usually a reaction to cancer cells that are still present and growing after prostatectomy, but this may have little to do with what is seen by NaF-PET/CT or bone scintigraphy, since both methods depict unspecific structural changes in osseous tissue that occur late in the development of skeletal metastasis and remain unchanged for a long time after the cancer may have disappeared, for instance due to effective chemo- or radiation therapy (*2,3*). Thus, it is time to realize that all imaging modalities demonstrating structural bone changes are not reliable harbingers of skeletal metastases and should be abandoned in favor of FDG-PET/CT and, when it comes to prostate cancer perhaps PSMA-PET/CT. Time will show which of the latter two approaches are preferable for showing bone marrow metastases in prostate cancer. However, in most other cancers, FDG-PET/CT will probably prevail for this purpose for reasons stated in detail elsewhere (*2,3*). Experts in nuclear medicine and molecular imaging should understand and communicate this, because otherwise how do we make co-operating surgeons and oncologists understand and act accordingly?

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