

## Tc-99m UBI Scintigraphy as a Cost-effective Alternative to Ga-68 NOTA-UBI PET/CT for Imaging Infections

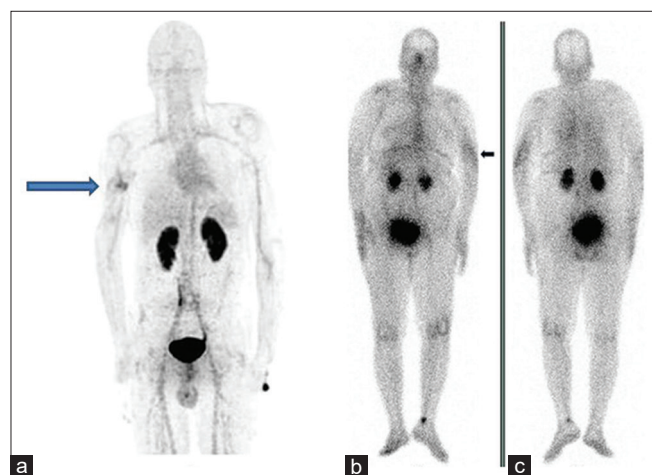
Sir,

Ubiquicidin (UBI) is an antimicrobial peptide with great potential for imaging infectious diseases. UBI can be labeled with  $^{99m}\text{Tc}$  and  $^{68}\text{Ga}$ , with NOTA acting as a bifunctional chelator for the latter.<sup>[1,2]</sup>

For  $^{68}\text{Ga}$  labeling, NOTA-UBI was labeled with  $^{68}\text{Ga}$ . We adapted the method described by Ebenhan *et al.*<sup>[3]</sup> and standardized the procedure for our department. For  $^{99m}\text{Tc}$  labeling, UBI was labeled with  $^{99m}\text{Tc}$  by a reduction method adapted from the method described by Arjun *et al.*<sup>[4]</sup> and standardized for our department.

The results of  $^{99m}\text{Tc}$ -UBI showed a labeling efficiency of  $97.46 \pm 1.06$  ( $n = 25$ ) in both mobile solvents, namely, saline and 5% HCl in methanol. Further,  $^{68}\text{Ga}$ -NOTA-UBI was also successfully labeled with a labeling efficiency of  $98.25\% \pm 1.32\%$  ( $n = 4$ ) in sodium citrate as mobile solvents. UBI labeling with  $^{68}\text{Ga}$ , and  $^{99m}\text{Tc}$  resulted in a clear and colorless solution with pH of 5 and 6, respectively. For labeling  $^{99m}\text{Tc}$ -UBI, heating was not required. However,  $^{68}\text{Ga}$ -NOTA-UBI labeling required heating at  $90^\circ\text{C}$  for 15 min.  $^{68}\text{Ga}$ -NOTA-UBI synthesis took a lesser time ( $18.15 \pm 1.3$  min) than the synthesis of  $^{99m}\text{Tc}$ -UBI ( $29.36 \pm 3.84$  min).  $^{99m}\text{Tc}$ -UBI and

$^{68}\text{Ga}$ -NOTA-UBI showed similar biodistribution in patients with suspected periprosthetic infection and satisfactory target to the nontarget ratio in true positive cases (one representative case each is shown) [Figure 1]. The cost of NOTA-UBI peptide was approximately Indian rupees 400,000/20 mg, thus allowing us to perform a theoretical maximum of 80 studies (250  $\mu\text{g}/\text{patient}$ ). However, our subsequent few studies revealed good biodistribution with 150  $\mu\text{g}$  of the peptide too, keeping a patient injected activity of 4 mCi; thus, the theoretical maximum cases could be about 130 cases. Even then, the cost of the peptide per patient came out to be approximately Rs. 3000.<sup>[5]</sup> The cost of UBI peptide for  $^{99m}\text{Tc}$  labeling was approximately Rs. 94,000/20 mg from which theoretically 400 syntheses can be done (50  $\mu\text{g}/\text{patient}$ ).<sup>[6]</sup> Thus, the cost of peptide per patient was approximately Rs. 3000 in NOTA-UBI and Rs. 230 in  $^{99m}\text{Tc}$ -UBI studies.  $^{99m}\text{Tc}$ -UBI and  $^{68}\text{Ga}$ -NOTA-UBI had similar biodistribution and depicted infection.  $^{99m}\text{Tc}$ -UBI requires a gamma camera setup and can be synthesized in-house as per requirement, whereas positron emission tomography (PET)/computed tomography (CT) facility and  $^{68}\text{Ge}/^{68}\text{Ga}$  generator are requirements for  $^{68}\text{Ga}$ -NOTA-UBI imaging. Overall, comparable labeling efficiency, similar biodistribution, satisfactory positive results, and cheap, ready availability make  $^{99m}\text{Tc}$ -UBI scintigraphy a practically useful imaging modality with a good cost-to-benefit ratio compared to  $^{68}\text{Ga}$ -NOTA-UBI PET, especially in the setting of limited resources. A prospective study with an adequate sample size is needed to establish our early results in comparing the two tracers.



**Figure 1:** (a)  $^{68}\text{Ga}$ -NOTA-ubiqualidin (UBI) whole-body positron emission tomography (metallic implants) image at 1 h, A 25-year-old man with a history of right nonunion humerus shaft fracture and operated multiple times (metallic implants). Tracer uptake was noted in the region of the mid-shaft of the right humerus with nonunion of the proximal and distal fragment with intervening tracer avid soft tissue (Blue arrow).  $^{99m}\text{Tc}$ -ubiqualidin anterior, (b)  $^{99m}\text{Tc}$ -UBI anterior whole-body images at 1 h, and posterior, (c)  $^{99m}\text{Tc}$ -UBI posterior whole-body images at 1 h, whole-body images at 1 h diffuse radiotracer uptake is seen in the lower one-third of the left arm reaching up to the elbow joint (peri-implant infection at the lower one-third left arm) in the above images (Black arrow)

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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