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LETTER TO THE EDITOR

The many roads to infection imaging

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Dear Sirs,

With great interest, we read the short comment of Giovanni Lucignani about infection imaging [1]. Here, commentaries are given, derived from a literature search including summaries of recently published articles. An important part of the publication was dedicated to the labelling of living bacteria with antimicrobial agents, mainly to the application of radiolabelled antibiotic ciprofloxacin for the specific detection of bacteria. Dr. Lucignani stated; "that the approach with technetium-labelled ciprofloxacin showed considerable promise in the preliminary studies but clinical trials have shown limitations".

On the contrary, most pre-clinical studies have shown poor specificity of technetium-labelled ciprofloxacin for bacterial infections [2–7] and vivid discussions related to this topic took place [8–10, 17]. One of the most tested radiolabelled ciprofloxacin is Infecton® (Draximage, Quebec, Canada). This compound was evaluated in the International Atomic Energy Agency (IAEA, Austria, Vienna) sponsored study of more than 500 patients and specificity was claimed for bacterial infections [11]. However, related to its specificity, other studies showed contradicting results in pre-clinical [2–7] and clinical settings as well [12]. Although it was suggested that this was due to sub-optimal labeling conditions and sample preparations, such statements could be easily refuted by routine radiochemical analysis and biodistribution studies in laboratory animals. More recently, claims for Infecton® in its specificity for detecting of bacterial infections in humans (depending on the discrepancy between early and late imaging) was refuted as well by Palestro et al., as his group conducted a Phase II trial sponsored by Draximage, the manufacturer of Infecton®, and they experienced that this tracer disappeared from sites of infection as well as from inflammation with equal rapidity [13]. As Infecton® shows detection of bacterial infections with poor specificity and accuracy [14], this group seriously considered that it is unlikely that radiolabelled antibiotics will ever be a viable method for imaging infection. Moreover, the recent press release from Draximage clearly stated that formulation development of Infecton® targeting orthopaedic indications has, to date, not been successful and Draximage will allocate the resources devoted to this product to other projects (http://www.draxishealth.com/pdf/Draxis_Q3_PR_US_GAAP.pdf). These findings are supported by two recent studies in which for synthetic ^{18}F-ciprofloxacin, no specific binding to bacteria was observed [15] and poor retention of this tracer in bacteria-infected tissues in patients [16]. These findings raise concerns about the specificity of radiolabelled antibiotics, especially for Infecton®, for the detection of bacterial infections. The issue of whether the uptake is not more than a blood pool effect or the non-specific penetration

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of radiolabelled ciprofloxacin through membranes of bacterial and mammalian cells as well may explain the conflicting findings [17, 18]. The rapid introduction of Infecton® in clinical settings may pointing out the necessity of the support of pre-clinical data and the analysis of radiochemical structure for any new radiochemical tracer dedicated to the detection of bacterial infections in clinical practice.

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