cannot be diagnosed in a single patient based entirely on the patient's medical records and conditions, as a firm examination including a skin biopsy must be undertaken. Robert F. Reilly reported that they might have missed milder presentations of NSF, or the clinicians may have missed full-blown cases of NSF [7].

In the FINEST study [8], which the authors are also mentioning in their comments, we find it interesting that, among the 308 patients included, none showed signs of cutaneous disorders within 4 months after MRI. These patients were all inspected by a physician, whereas no experienced dermatologist with hands-on experience was involved. Furthermore, they reported their retrospective inclusion period between July 2005 and July 2006, with a follow-up of 4 months. However, speculations could be drawn that NSF cases (if any) had not been established during these few months.

With regard to the Varani [9] *in vitro* study of human dermal fibroblasts in monolayer culture, it was reported that gadodiamide, gadopentetate, gadobenate and gadoteridol all caused persistent, increased fibroblast proliferation and increased production of the regulators of collagen turnover [matrix metalloproteinase-1 (MMP-1) and tissue inhibitor of matrix metalloproteinase-1 (TIMP-1)]. This suggests that all GBCAs may stimulate the same fibrotic processes in human tissue at high concentrations.

We recognize that today's list of NSF cases is highest for the linear-structured gadolinium-chelated agents, but based on our study, we strongly believe that gadobutrol could be involved in the development of NSF in a way similar to those reported involving other gadolinium-containing agents. Thus, we feel that macrocyclic agents may currently not be considered as a safe MRI agent for renal impaired patients.

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Twinkling sign?

Recently, Andrulli *et al*. [1] published a study about twinkling artefacts. The authors suggest that one should not speak of 'twinkling artefacts' but rather of 'twinkling signs', as this phenomenon plays an important role in kidney stone diagnosis. Both twinkling artefacts [2] and urine jet have been identified for many years but little used for purposes of diagnosis. Unlike other countries, in Switzerland, these phenomena were introduced by Jürg Prim into the course catalogue of the learning objectives for abdominal sonography training as early as 2003.

In fact, the search for stones in the renal sinus and in the ureter is not easy. Previously, the sensitivity of ultrasonography to ureteral stones was low with only 19–37% reported [3]. Thanks to the twinkling artefact, kidney stone diagnosis has been greatly enhanced. In addition, many ureteral stones and also renal sinus stones have been discovered. Our prospective study [4] showed that, with the combined utilization of twinkling artefacts, modern equipment and indirect signs of a stone, sensitivity, comparable with CT, of 98.2% and specificity of 100% were achieved. More recent studies by Park *et al*. [5] achieved a sensitivity of 93 and 98.5%, respectively, and specificity of 95 and 100%, respectively. In the study by Park *et al*. [5], twinkling in 184 of 214 stones was detectable (86%).

Indirect signs of nephrolithiasis are important, and here, urine jet plays an important role. A normal value is two jets per ureter per minute. The measurements are carried out between 3 and 5 min. But the twinkling artefact arises not only from renal stones, it also exists in many other formations with hard echoes. For example, some of these formations include calcifying pancreatitis or colonic air. Because twinkling is not specific only to urethral stones, I think that we should continue to speak of twinkling artefacts, and not, despite its usefulness, of twinkling signs.

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Reply

We thank Tuma for his valuable comments on the issues underlined in our case report 'Colour Doppler twinkling in kidney stones: artefact or sign?' [1], supporting the value of twinkling and of ureteral jet in the diagnosis of urinary stones. We agree that, until now, the twinkling has not been adequately evaluated and specified in the standard reporting of urinary ultrasonography of patients suspected with urinary stones. The main difficulties in the dissemination of its use in everyday practice can be due to different causes: firstly, the knowledge of the phenomenon in the radiological community seems to be fragmentary; secondly, the kidneys and the urinary system need to be explored with colour mode after B-mode examination; and finally, it requires a particular type and setting of instrumentation to see easily the twinkling in a reproducible manner [2]. In addition, the new ultrasound probes have a tomography-like capability that has reduced the twinkling appearance compared with the oldest ones. From a purely technical point of view, the twinkling remains an artefact that is useful to unmask false blood flows, but we have 'provocatively' used the term 'sign' to underline, from the clinical point of view, its positive diagnostic value. In fact, the usefulness of artefacts in the diagnostic echographical work-up is already well known, i.e. when a clear acoustic shadowing distal to an echogenic focus in the gallbladder leads us to the diagnosis of gallstones: it is an artefact but is an important 'sign' because it improves and increases all the information necessary to get a more accurate diagnosis.

Finally, in our experience, there is no evidence that twinkling arising from the colon derives from air or faecal material or both, in contrast with some metastatic calcifications of soft tissues like occurring in aortic, carotid, and femoral arteries or prostate or stones within a polycystic kidney (Figure 1).

In conclusion, the twinkling is a technical artefact, which is a clinically useful but not specific sign of urinary stones and/or calcifications that needs to be more widely known in the nephrological and urological specialties.

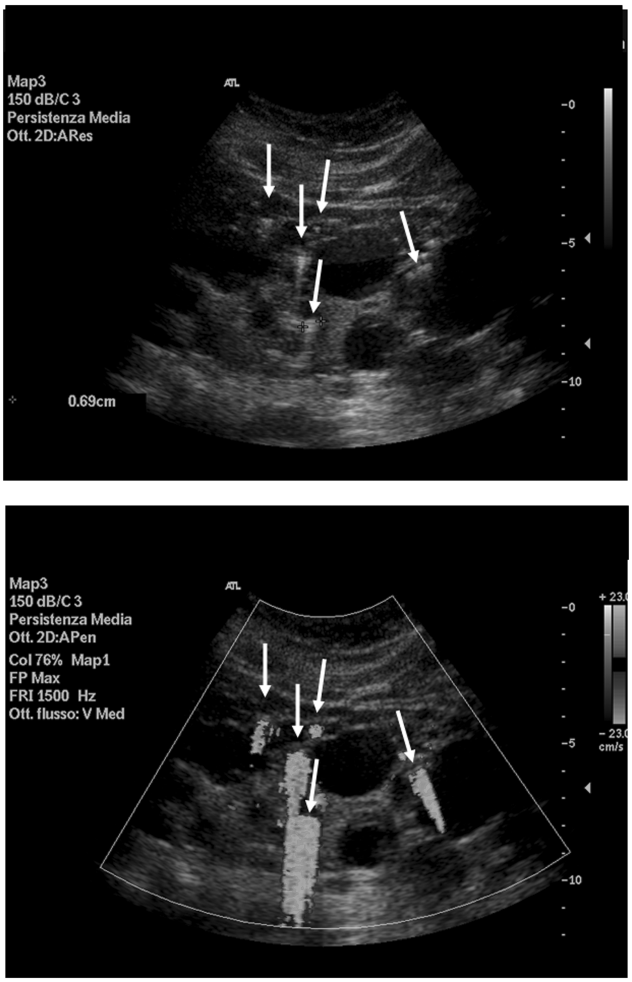

Fig. 1. Twinkling of kidney stones within a polycystic kidney at colour-mode examination.

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