The risk of serious bleeding due to kidney biopsy in patients with myeloma is likely to be increased because myeloma-associated with a bleeding diathesis (as the authors note). Indeed, the largest and most recent trial of plasmapheresis for myeloma-associated kidney failure did not specify kidney biopsy as an inclusion criterion because of concerns about the risks vs benefits of the procedure [2].

Can the authors specify how a biopsy result will—in many patients—sufficiently alter management beyond standard measures (such as volume expansion, control of hypercalcaemia, chemotherapy) to justify its increased risk? One answer might be that demonstration of the presence of acute cast nephropathy would prompt initiation of plasmapheresis. However, the largest trial of myeloma-associated acute renal failure did not show a clear benefit with this invasive therapy [2].

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Reply

Sir,

Dr Magee wonders why patients with a myeloma-associated kidney disease should have a kidney biopsy [1] as he doubts that biopsy results will alter management in these patients justifying the increased risk of bleeding.

In patients with myeloma, renal lesions are heterogeneous and combined pathological lesions may be found. In autopsy series, cast nephropathy is the most common lesion but AL-amyloidosis (not diagnosed pre-mortem) and light chain deposition disease were also found [2]. Forty-five percent of the patients had more than one finding. Besides the diagnosis, renal histology gives information about fibrosis, tubular atrophy, and may help to assess the chance of recovery. In a long-term outcome study, Montseny et al. [3] underlined the value of initial renal biopsy. They found that histology predicts prognosis. In their report, only 41% of the patients were identified as myeloma kidney, whereas AL amyloidosis or light chain disease was found in nearly half of the remaining cases. Patients with light-chain deposition disease (underestimated when biopsy is not performed) had the best prognosis. Renal diagnosis will alter treatment decisions in some patients. Taking into account the poor prognosis of AL amyloidosis, the use of high-dose chemotherapy and autologous stem-cell support will be restricted to very few patients. As Dr Magee stated, plasmapheresis has not shown any benefit in a recently published randomized trial [4]. However, the authors themselves discussed the limitations of their study, one of them, the missing renal biopsy, as an inclusion criterion.

Dr Magee has stressed an important point: the increased risk of bleeding in patients with myeloma. This has been found in patients with amyloidosis [5], and may be due to amyloid-associated factor X deficiency or the deposition of amyloid either in the vessel wall or in the perivascular region. However, biopsy studies of Hergesell et al. [6] and Manno et al. [7] did not report an increased incidence of major complications nor did Magee et al. in 21 patients with myeloma [8]. Nevertheless, there must be a clear awareness of the bleeding tendency in those patients (history of bleeding, haematomas at examination, abnormal coagulation tests) not to further increase the risk by performing a kidney biopsy.

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Markers of bone turnover in haemodialysis patients

Sir,

I read with interest the article by Albalate et al. [1] on the association between phosphate removal and markers of bone turnover in haemodialysis patients. I would like to report our
Table 1. Serum markers of bone metabolism in dialysed patients

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<tr>
<td>iPTH, pg/ml</td>
<td>109.2 (13.7–334.9)</td>
<td>199.9 (10.3–1266.9)</td>
<td>429.7 ± 379.6</td>
</tr>
<tr>
<td>CAP (1-84 PTH), pg/ml</td>
<td>79.2 (9.3–238.6)</td>
<td>126.7 (6.5–887.9)</td>
<td>353 ± 350</td>
</tr>
<tr>
<td>CIP (7-84 PTH), pg/ml</td>
<td>48.4 (2.4–129.0)</td>
<td>70.4 (3.3–398.9)</td>
<td>76.7 ± 79.8</td>
</tr>
<tr>
<td>tAP, U/l</td>
<td>64 (60–98)</td>
<td>122 (74–577)</td>
<td>138.7 ± 130.1</td>
</tr>
<tr>
<td>OPG, pmol/l</td>
<td>4.0 (2.1–13.4)</td>
<td>7.8 (1.5–15.8)</td>
<td>16.2 ± 12.5</td>
</tr>
<tr>
<td>OPGL (RANKL), pmol/l</td>
<td>2.1 (0.0–5.3)</td>
<td>0.6 (0.0–10.0)</td>
<td>1.03 ± 1.02</td>
</tr>
<tr>
<td>OPGL/OPG (RANKL/OPG)</td>
<td>0.73 (0.00–1.60)</td>
<td>0.10 (0.00–1.45)</td>
<td>0.08 ± 0.1</td>
</tr>
</tbody>
</table>

Results are presented as: a median and range; b mean ± SD.

CAP, cyclase activating parathyroid hormone; CIP, cyclase inactive parathyroid hormone; HD, haemodialysis; iPTH, intact parathyroid hormone; OPG, osteoprotegerin; OPGL, osteoprotegerin ligand; PD, peritoneal dialysis; tAP, total alkaline phosphatase.

own experience with determination of osteoprotegerin (OPG)—receptor activator of nuclear factor (NF)-κB (RANK), its ligand (OPGL, RANKL) and other serum markers of bone metabolism and relate our results to those shown by Albalate et al. [1]. To my understanding, Dr Albalate is not familiar with our data.

In our uraemic patients treated with peritoneal dialysis (PD) or haemodialysis (HD), serum OPG level was higher than in controls. PD patients showed lower OPG level than HD ones [2–4]. OPG concentration was elevated in 92.7% of HD patients and in 51.7% of PD ones [2,4]. OPGL (RANKL) was in our study lower in HD patients than in controls [3,4]. The same pattern of changes was shown for the OPGL/OPG ratio [3,4].

Results of selected serum markers of bone metabolism, obtained in our dialysed patients and in those described by Albalate et al. [1], are shown in Table 1. Patients, presented by Albalate et al. [1], have higher serum OPG level and lower OPGL/OPG ratio as compared to our patients. These differences may be explained by serum concentration of parathyroid hormone (PTH) levels (intact PTH—iPTH, 1-84 PTH – CAP, 7-84 PTH – CIP). The lowest serum OGP levels and the highest OPGL/OPG ratios were shown in PD patients, having the lowest serum levels of PTH. In the whole group of our examined patients (PD and HD), serum OPG level correlated positively with iPTH (R = 0.374, P = 0.019), CAP (R = 0.366, P = 0.022) and CIP (R = 0.406, P = 0.010). Serum OPGL level correlated negatively with iPTH (R = −0.377, P = 0.018), CAP (R = −0.356, P = 0.026) and CIP (R = −0.383, P = 0.016); the same pattern of correlations was shown for the OPGL/OPG ratio (R = −0.435, P = 0.006 for iPTH; R = −0.414, P = 0.009 for CAP; and R = −0.440, P = 0.005 for CIP). From our results, we concluded that when serum PTH increases, OPG also rises to prevent bone destruction associated with PTH action [3].

PD patients are more predisposed to adynamic bone disease (ABD) than HD ones [5]. We lean towards the hypothesis that a lower serum OPG level is connected with lower activity of osteoclasts, than that which appears in ABD [6] and with less compensating production of OPG [2]. Albalate et al. [1] have speculated that OPG increases in HD patients as a compensatory mechanism, in an attempt to compensate the enhanced resorptive activity in secondary hyperparathyroidism. This possible explanation is in agreement with our concept. However, when dialysed patients were separated using iPTH concentration below or over 100 pg/ml, there were no significant differences in serum OPG, OPGL and the OPGL/OPG ratio between both groups [7].

Albalate et al. [1] have found positive correlation of OPG and age in HD patients; in our study dialysed patients over 65 years had higher serum OPG level than those at an age less or equal to 65 years [8]. We think that an increase in serum OPG in older patients probably reflects a paracrine mechanism of bone cells to compensate for age-dependent bone loss.

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