Case Report:
Nonsecretory Multiple Myeloma MRI Monitoring of Therapy Response

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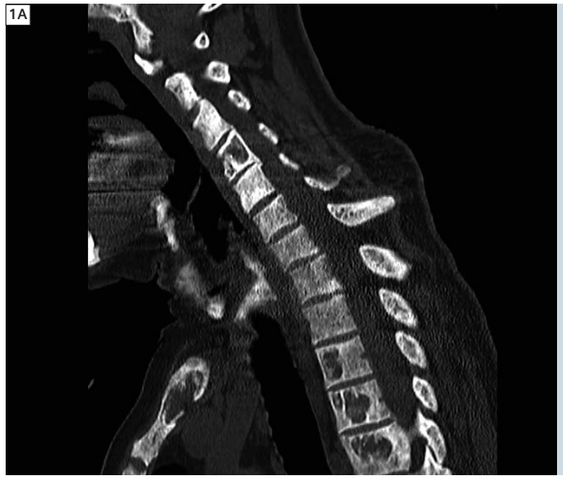
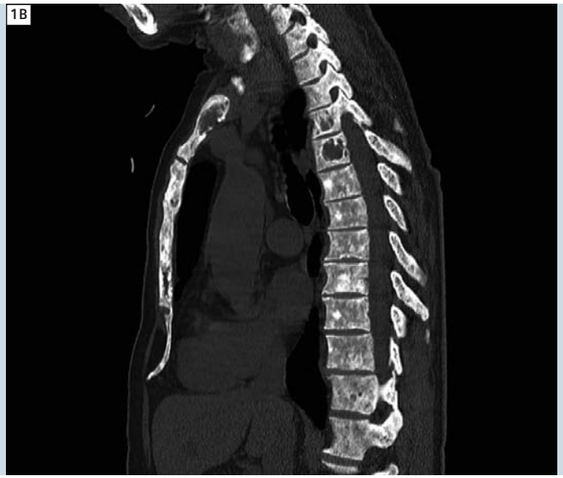
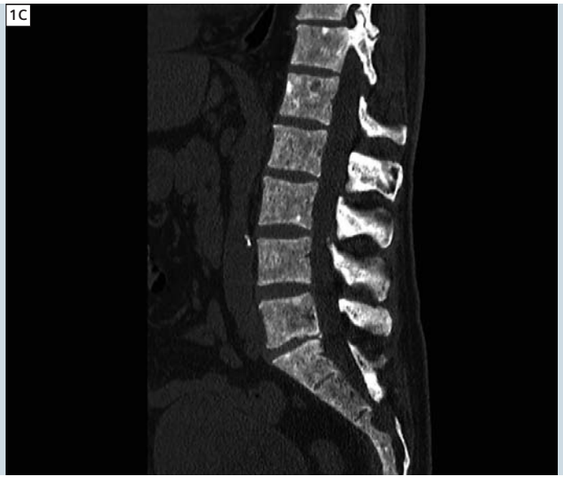
Multiple myeloma (MM) is a malignant hematologic disorder characterized by the infiltration of neoplastic plasma cell into bone marrow. Detection of medullary involvement is best accomplished with the aid of MRI. Nevertheless, assessment of myeloma bone disease consisting of bone destruction due to increased activity of osteoclasts generally not accompanied by a comparable increase of osteoblasts function and consequently by new bone formation, is the hallmark of MM. Thus, competing imaging modalities are nowadays used for optimal patient management.

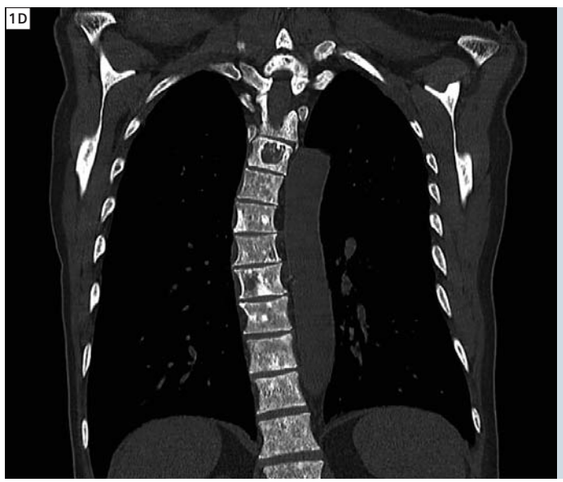
With the event of novel antimyeloma therapies, imaging monitoring, in addition to classical hematologic monitoring, has been advocated by many authors. Visualization of myeloma burden at baseline and during therapy is beneficial for more accurate patient management and prognostic evaluation. Therefore, whole-body imaging protocols are mandatory, especially for assessment of myeloma infiltration in all bone marrow cavities (medullary involvement) as well as for diagnosis of extramedullary involvement. These two myeloma manifestations can be displayed at best by joined multi-detector Computed Tomography (MDCT) and MR imaging. Nonetheless, as we generally have to avoid IV contrast application, due to impaired renal function, evaluation of myeloma activity at follow up alone by means of nonenhanced studies (conventional imaging) proves generally difficult. Moreover, in some cases, medullary myeloma cell infiltrates do not entirely regress at time. With MRI, besides signal intensity abnormalities occurring during therapy, contrast enhancement is the sole finding in support of residual tumor vitality. At this point, the use of diffusion-weighted MRI could represent a practicable alternative to contrast studies or even tumor perfusion studies. The main informational gain from this approach could hence represent a much more accurate differentiation between new active and older inactive lesions which is otherwise not possible to detect with confidence, other than by using, for instance, additional functional imaging techniques such as FDG-PET.

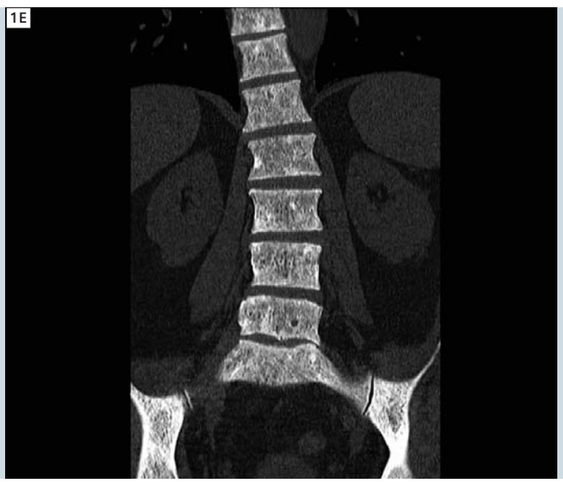


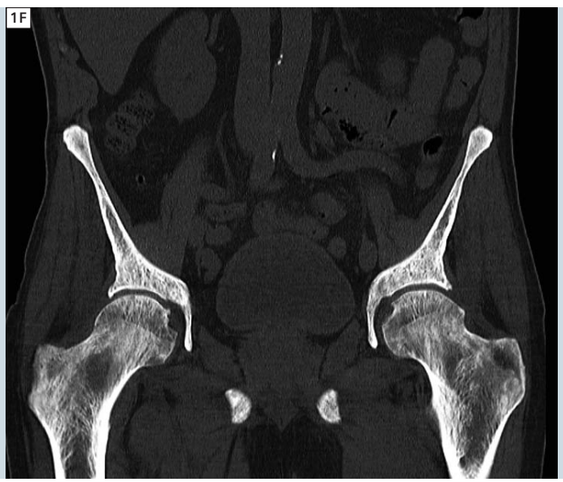




1 Low dose MDCT used for evaluation of myeloma. In the shown case, osteoscleroses is evident as well as multiple lytic lesions. Additionally medullar infiltration is present. **1A, B, C**: Sagittal reformation of MDCT (**A** cervical, **B** thoracic, **C** lumbar spine).



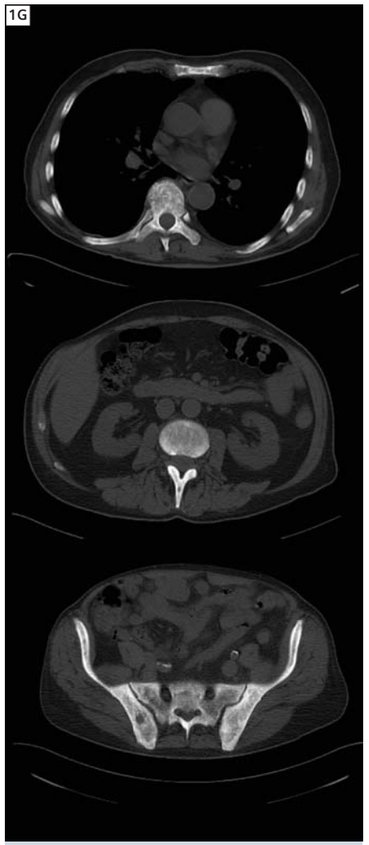




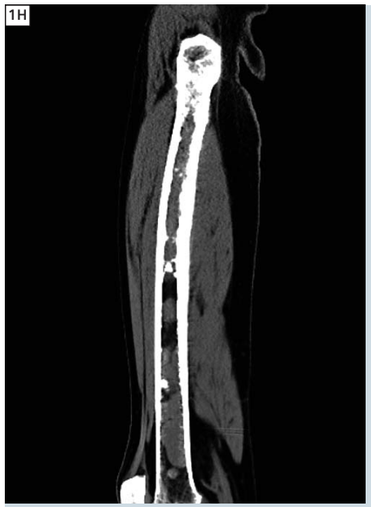
1 **1D, E, F**: Coronal MPR (**D** thoracic, **E** lumbar **F** pelvis).

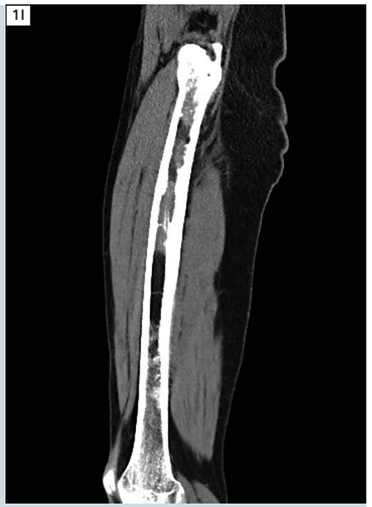
We report in this case on a 73-year-old male patient with a nonsecretory multiple myeloma; the first manifestation of the disease with pathologic fracture of the clavicula was reported in 1996, however, definitive diagnoses of nonsecretory myeloma was two years later in 1998 after multiple frustrane bone biopsies. Histopathology revealed at this time point a high degree of osteoscleroses with infiltration of lymphocytes and plasma cells. The patient was treated initially with an Alexanian chemotherapy regimen (Melphalan and Prednison) and stayed for six years in good partial remission. Besides initial bone sclerosis, sclerosis of cancellous bone increased after therapy, hampering in part evaluation of bone marrow signal and CT-attenuation acquired for imaging surveillance.

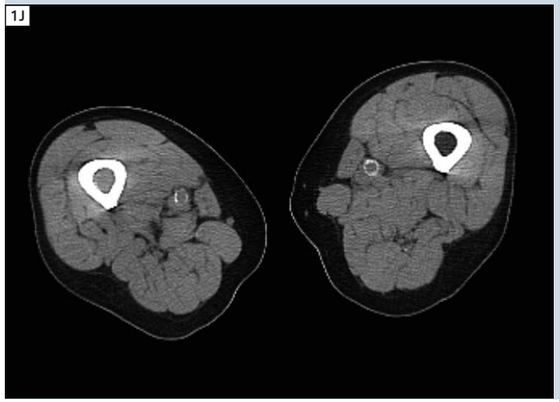
At the time-point of presentation at our department for the whole body (wb) imaging detailed in this report, the patient received a long-term maintenance chemotherapy after successful therapy of tumor progression (histology: bone marrow infiltration of 95%) with normalization of Hb-levels in 2008. At the time-point of wb MRI, the patient had



1 **G:** Original MDCT data sets (bone window).





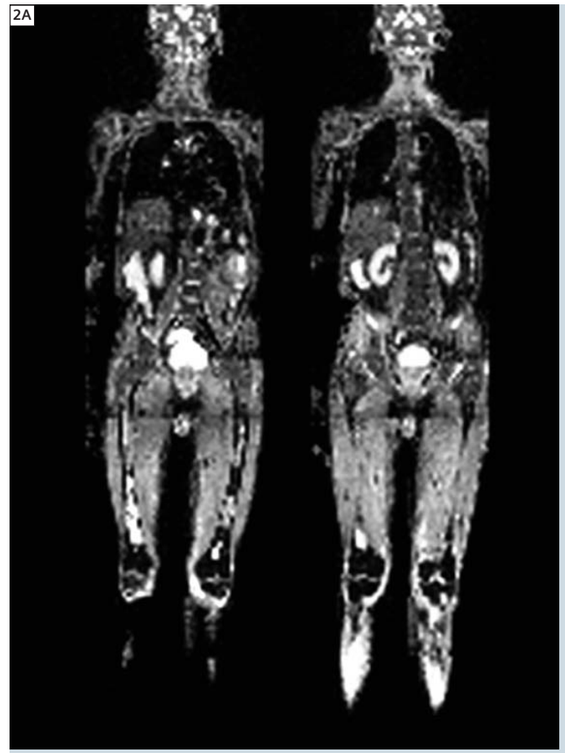


1 **H–J:** Visualization of bone marrow (**H** right, **I** left femur in oblique sagittal view).

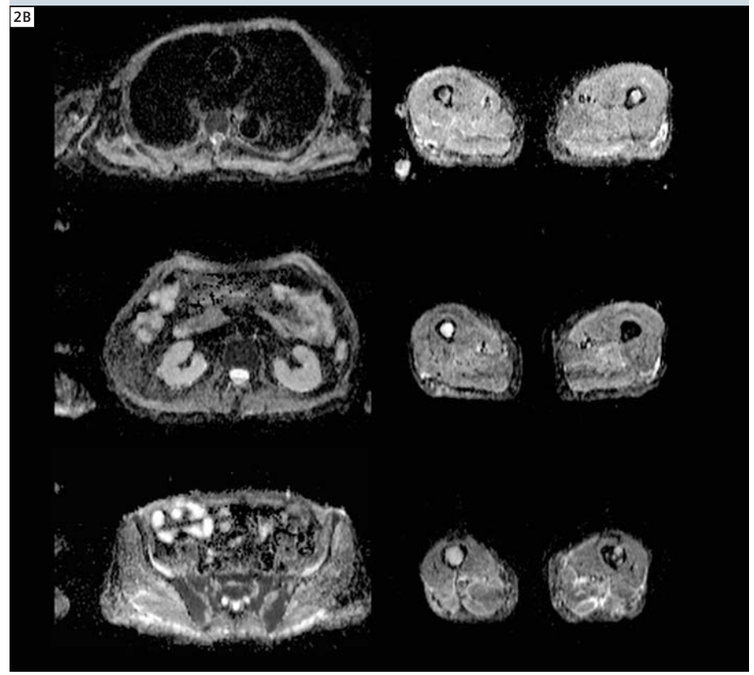
been suffering from progressing dyspnoea for one week, with diminished appetite and adynamia. Also in line with the reduced general condition, slight lost of weight was documented (3 kg over the last three months). Blood parameters showed now anaemia, which was initially suspected to be mainly caused by chemotherapy scheme, and additionally infection parameters were positive. Therefore the patient received blood transfusion and antibiotics for symptomatic therapy. With the exception of a slight swelling of one ankle, inspection and vital parameters were normal; the patient also received long-term anticoagulation therapy because of former deep vein thromboses, although, D-Dimere were in normal range and no thromboses (Ultrasound (US) of the extremities) or pathologies of the lung (MDCT scan) were present at the time point of presentation. For evaluation of potential further progression of the non-secretory myeloma, a low-dose whole body CT scan follow-up was initially performed. This scan showed the already known scleroses of the bones with emphasis of the vertebrae and pelvis (Figs. 1A–G). However, a reduced density of medullar infiltration was reported while comparing the results with former wb MDCT scans (not shown). Nevertheless, medullar tumor foci were still present (Figs. 1H–J) and therefore residual tumor activity was diagnosed based on MDCT. There was no evidence, however, for a progression of the lytic lesions and no static hazard was reported. While low-dose wb MDCT has to be considered as the standard care for myeloma and is clearly superior to conventional x-ray, especially in case of nonsecretory myeloma, information of diffuse bone marrow infiltration is best provided by MRI. Therefore the patient was referred for a wb MRI.

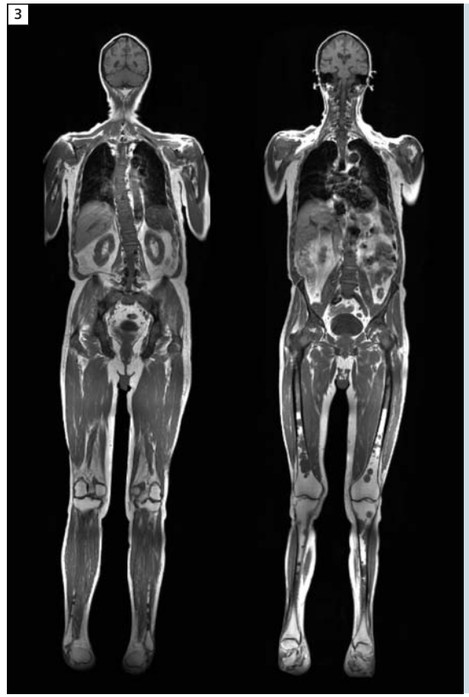
Our myeloma protocol at 1.5 Tesla (MAGNETOM Avanto) includes coronal T1-weighted (T1w) and T2w TIRM images and whole-body diffusion-weighted imaging (DWI). Sequence parameters for single-shot EPI DWI (*syngo* REVEAL) were: TR / TE = 4500 / 59 ms, spectral fat suppression, slice thickness 4 mm, 4 averages, 192 matrix, PAT (*syngo* GRAPPA) factor of 2, averaged 3-scan trace at b-values of 50 and 800 s/mm^2, bandwidth 1530 Hz/Px, 30 slices per step; in total 13 positions had to be acquired in this patient. With a measurement time of approximately 2–3 min per step including automated shimming, a total measurement time for wb DWI of approximate 33 min resulted in this case. No contrast media was applied, for either CT or MRI. For comparison with coronal T1w and TIRM images, transversal acquired DWI images were reformatted and displayed in multiple oblique orientations with the *syngo* 3D task card; ADC-maps were generated automatically with the scanners integrated software (Inline Diffusion tool).

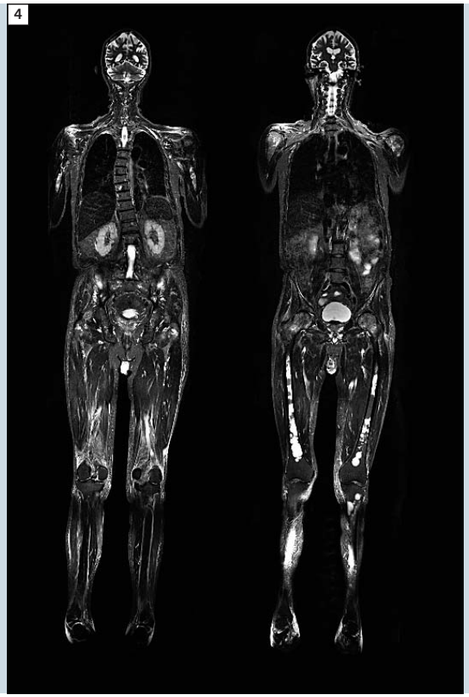
Based on morphology only, the MRI findings would be suggestive of high tumor load with special focus on the femora. Taking into account only the high b-value images, this diagnosis would be supported by DWI. However, based on wb ADC-mapping, a completely different picture became evident. Based on the high ADC values, high signal on the original b-value images had now to be interpreted as T2-shine through effect and not as a restriction of diffusivity. On the first look, this seems to contradict the results of the MDCT scan, where multiple nodules within the yellow marrow are present (compare figures 1H–J). But on the ADC-maps, different areas with high and very low diffusivity can be detected within the bone marrow of the femora as well as in the tibial bones; this indicates the presence of nodules with viable tumor, but the vast majority of these medullary findings have to be interpreted as transformed bone marrow after therapies with necrotic areas. T1w imaging, and especially DWI shows also remarkable dense bone marrow and / or tumor infiltration of the vetebra and pelvic bones. The high signal in original b-value imaging in combination with very low ADC values in particular is a clear indicator of high cellularity within



2 **A:** Multiplanar reconstruction (MPR) in coronal view of whole-body ADC images.
B: Transversal ADC-maps.

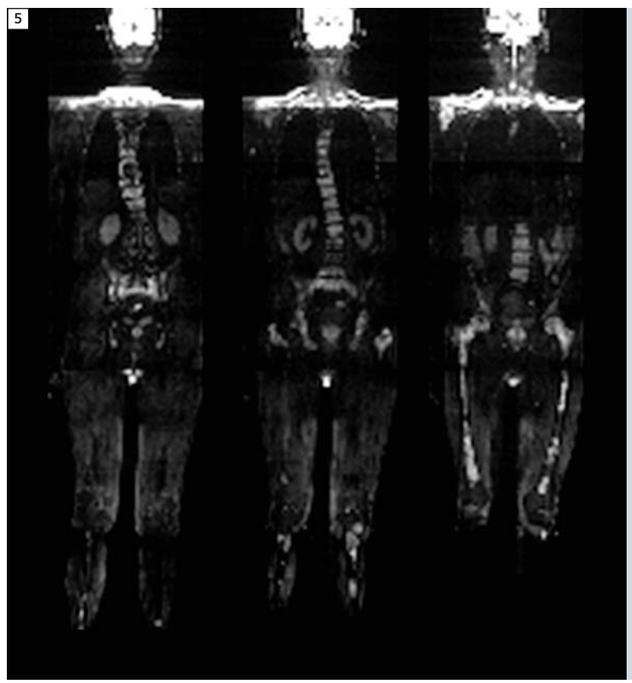


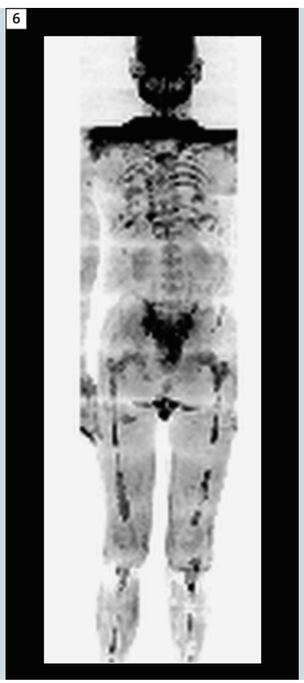




3 Corresponding whole-body T1w MRI.

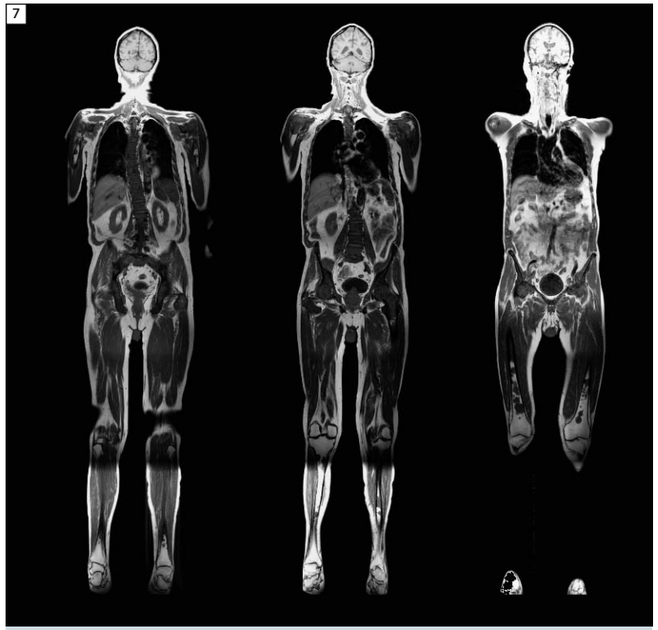
4 Corresponding whole-body T2w TIRM MRI.



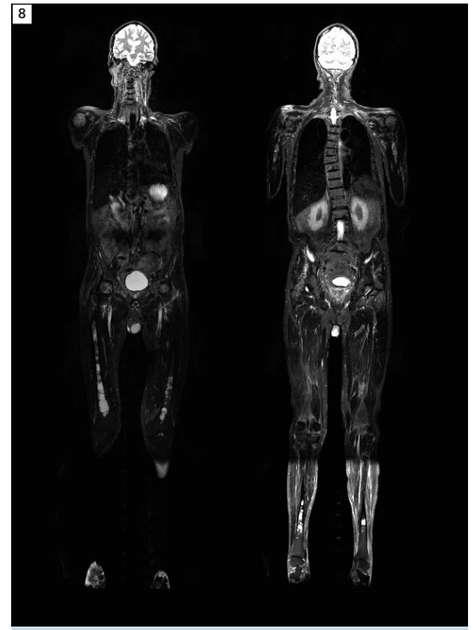


5 MPR of original b-value images in coronal view ($b = 800\ s/mm^2$).

6 Inverted maximum intensity projection (MIP) of $b = 800\ s/mm^2$ images.



7 Short-term follow-up, T1w MRI.



8 Short-term follow-up, T2w TIRM MRI.

the bone marrow; without DWI the signal lost on T1w MRI could also be interpreted as high density of bone matrix. Of course a definitive separation of myeloma infiltration and hyperproliferative / compensating hematopoietic system is challenging, given also the information provided by functional (DWI, perfusion) and metabolic imaging, and will be a challenge also for bone marrow biopsies. In this particular case, the patient's history and symptoms did support the MR diagnosis of tumor progression. The short-term follow up (Figs. 8–10) with MRI showed a tendency to progression of the nonsecretory myeloma.

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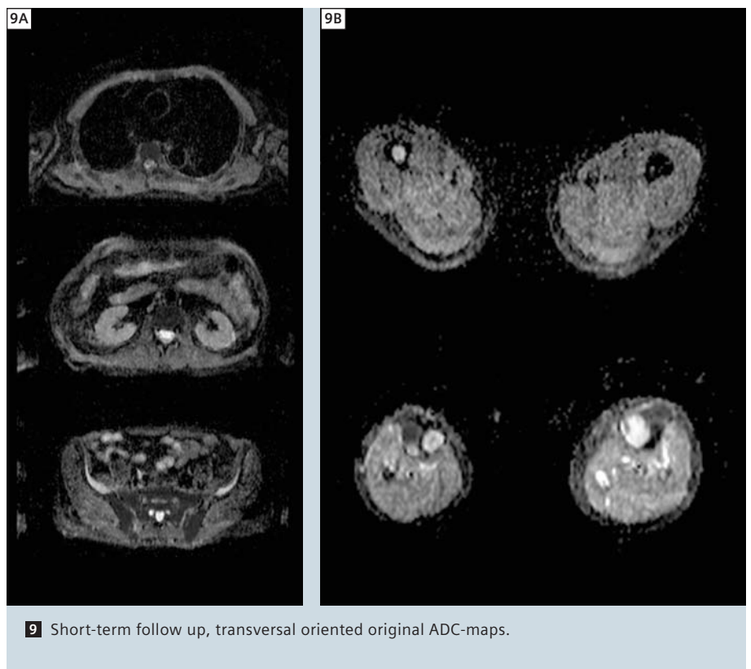

9 Short-term follow up, transversal oriented original ADC-maps.