abnormalities on ^{18}F-FDG PET, sometimes in the absence of abnormalities on conventional radiological modalities. Rituximab is an important drug in the treatment of NHL patients; its withdrawal should, therefore, only be considered in symptomatic patients. RP proved to be reversible after discontinuation of rituximab in combination with administration of steroids or supportive care. More research has to be performed to confirm and quantify the association of rituximab and adverse lung reactions, to understand the underlying mechanism and to search for variables, predisposing for the development of RP.

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FDG-positron-emission tomography for staging and therapeutic assessment in patients with plasmacytoma

Plasmacytoma can be confined to bone (solitary bone plasmacytoma) or occur in extramedullary sites (extramedullary plasmacytoma).[1-4] Diagnostic criteria are a biopsy-proven lesion of bone or soft tissue with evidence of clonal plasma cells, normal bone marrow with no evidence of clonal plasma cells and absence of end-organ damage.[5,6] In a recent study, Zamagni *et al*. have shown that although MRI of the spine and pelvis still remains the gold standard imaging technique for the detection of bone marrow involvement in multiple myeloma, FDG-PET/CT provides additional and valuable information for the assessment of myeloma bone disease in areas not covered by MRI.[7] The purpose of the present study is a prospective comparison of FDG-PET/CT and MRI for the appraisal of the staging and the therapeutic assessment of patients with plasmacytoma.

Twenty-four patients (17 males and 7 females; median age 60 years, age range 35-78) with pathologically documented plasmacytoma were included from June 2003 to June 2007 at the University Hospital of Nantes (France). Patients underwent whole body FDG-PET/CT (also covering skull, upper and lower limbs) and bone marrow MRI at the initial staging and therapy afterwards. The physicians for the therapeutic assessment knew the primary site of the disease. For both ethical and practical reasons, not every suspected involved lesion was evaluated by histology. When histological data were not available, the gold standard, therefore, resulted from an exhaustive analysis of patient data and follow-up.

Twenty-three patients were assessed for pre-therapeutic staging and 14 for therapeutic staging. At baseline staging, 54 tumor sites were confirmed according to the gold standard: 50 in bone areas and 4 in soft tissue areas (head and neck, breast and pelvis).

For the baseline staging, overall 460 regions in 23 patients were analyzed by FDG-PET/CT and 120 regions in 20 patients compared to MRI. FDG-PET/CT showed abnormal uptake in 57 sites (53 in bone areas and 4 in soft tissue areas): 53 foci considered as true-positive (TP) and 4 foci as false-positive (FP). FDG-PET/CT missed 1 lesion (iliac bone) confirmed by biopsy. In the 120 regions explored by MRI, 29 lesions were confirmed as being plasmacytoma, according to the gold standard. MRI detected 32 abnormal images, 27 images considered as TP and 5 as FP. MRI missed 2 lesions. FDG-PET/CT correctly classified the 5 FP and the FN. In those areas, FDG-PET/CT showed 3 foci considered as FP and missed 1 lesion, all correctly classified by MRI. Se, Sp, PPV and PNV were calculated. Results are shown in Table 1.

The accuracies of MRI and FDG-PET/CT in detecting lesions were concordant in 12/20 patients (60%) and discordant for the remaining 8/20 (40%). Finally, in 10/20 patients (50%), FDG-PET/CT detected plasmacytoma lesions in 18 areas (bone: 8 patients, soft tissue: 2 patients), which were outside the scope. Figure 1 shows a lombar spine plasmacytoma detected by FDG-PET/CT and MRI.

For therapeutic evaluation, 14 FDG-PET/CT, corresponding to an overall 260 regions, were analyzed; 10 FDG-PET/CT (61 regions) compared with MRI. Five patients have been treated by radiotherapy, 6 by chemotherapy and 3 by high-dose chemotherapy and autologous stem cell transplantation. A complete response was observed in the 5 radiated patients and in 2 patients treated by chemother-

Table 1. FDG PET/CT and magnetic resonance imaging performance for staging and therapeutic assessment.

	Baseline staging		*Therapeutic assessment*	
	FDG PET/CT n=460	*MRI n=120*	*FDG PET/CT n=260*	*MRI n=61*
Se	98% (53/54)	93% (27/29)	100% (18/18)	100% (9/9)
Sp	99% (402/406)	94% (86/91)	99% (241/242)	89% (46/52)
PPV	93% (53/57)	84% (27/32)	95% (18/19)	60% (9/15)
NPV	99% (402/403)	98% (86/88)	100% (241/241)	100% (46/46)

n: number of analyzed anatomical sites.

apy, only a partial response in 4 and none in 3 for the other patients. FDG-PET/CT showed persistent abnormal uptake in 18 sites, all in bone, and disease was confirmed for all these sites. Among the 61 regions compared using both FDG-PET/CT and MRI, the findings were concordant for 9 positive and 45 negative areas and discordant for 7 regions in 3 patients. As a matter of fact, MRI falsely classified 6 positive lesions, each of them being correctly classified by FDG-PET/CT (Figure 1). Se, Sp, PPV and PNV are given in Table 1.

FDG-PET/CT is a metabolic imaging technique where the scope covers the whole body (from skull to lower limbs). Major advantages of FDG-PET/CT are the ability to perform full body examinations, the potential to detect medullary and extramedullary lesions in one single examination and the possibility of distinguishing new active disease from scar or necrotic tissue. Studies comparing FDG-PET with conventional techniques for plasmacytoma detection have been limited due to the rareness of the disease. To the best of our knowledge, the present study is the first one conceived to assess FDG-PET/CT prospectively in a *relatively large* series of plasmacytomas for initial staging and therapeutic appraisal. In addition to this, we compared the performance of FDG-PET/CT to that of MRI in most cases. Our results show that FDG-PET/CT has a high performance for initial staging of plasmacytoma. Its performance seems equivalent to that of MRI in spine and pelvic bone. Thus, FDG-PET/CT allows investigation with a larger scope, e.g. soft tissues, skull, ribs and limbs. During initial staging, MRI missed 18 lesions located outside of the scope. Moreover, FDG-PET/CT shows a higher performance than MRI for therapeutic assessment. Indeed, MRI failed to differentiate scars from persistent active lesions, as previously observed for multiple myeloma.[7] Our study found a higher performance for plasmacytoma assessment than that published for multiple myeloma.[7-10] This is probably due to the generally larger size of usual plasmacytoma lesions. Furthermore, we used a hybrid system of PET integrated with CT, which allows for an exact detection of small and/or slightly active lesions. Such lesions are not easily recognized nor differentiated from soft tissue lesions, when using PET alone. In addition, by means of fused images, where each hypermetabolic lesion was concordant with the morphology of a lesion on the corresponding CT image, we could directly confirm the reliability and specificity of our FDG-PET/CT findings in all patients.

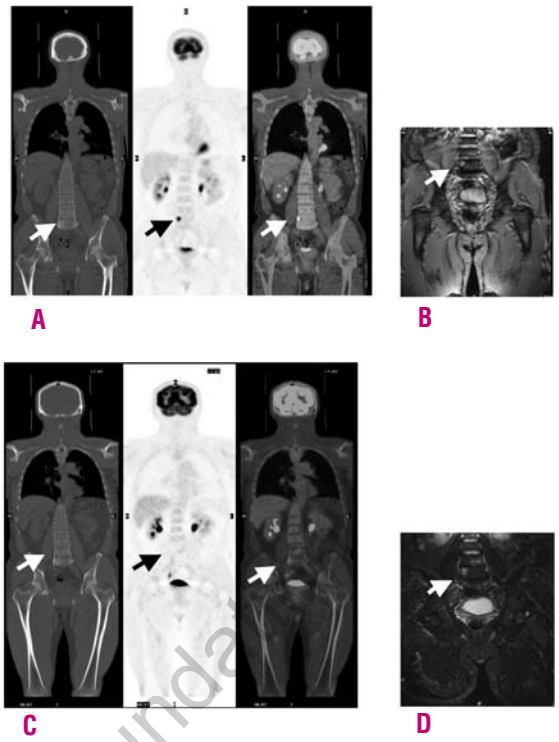

Figure 1. Images performed on a 49-year old male with a lombar plasmacytoma. Before treatment, plasmacytoma was detected by FDG PET/CT (A) and MRI (B). After external radiotherapy, FDG PET/CT (C) revealed no abnormal uptake. MRI (D) showed a persistent abnormal spine signal. Follow-up confirmed the absence of recurrence.

In conclusion, PET-CT proves to be a technique that can be used for the widespread screening of plasmacytoma lesions, both in bone and soft tissues in clinical practice. It can probably also be used to assess therapeutic efficiency.

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Clonal chromosome anomalies and propensity to myeloid malignancies in congenital amegakaryocytic thrombocytopenia (OMIM 604498)

Congenital amegakaryocytic thrombocytopenia (CAMT, OMIM 604498) is an autosomal recessive disorder characterized by absent or reduced number of megakaryocytes in the bone marrow (BM) since birth, elevated serum levels of thrombopoietin (TPO), and very low platelet count. Prognosis of CAMT patients is poor, because all develop in childhood a tri-linear marrow aplasia that is always fatal when untreated.[1,2] Mutations of the *MPL* gene (OMIM 159530), coding for the TPO receptor,[3] are responsible for CAMT.[4,5] We report the cytogenetic investigations and the results of analysis by fluorescent *in situ* hybridization (FISH) on 5 unrelated Italian patients whose clinical characteristics and *MPL* gene mutations have already been reported.[5] Three patients were females and two males, age at diagnosis ranging between 16 and 49 months. All children developed pancytopenia at an age comprised between 22 and 49 months. Patients' designation (CAMT1-CAMT5 in Table 1) is as in Savoia *et al*.[5]

Chromosome analyses were repeatedly performed on BM and peripheral blood (PB) PHA-stimulated cultures with routine methods. Skin fibroblasts (SF) were cultured with routine methods in patient CAMT2. QFQ-banding technique was used for all chromosome analyses. FISH analyses on interphase nuclei were repeatedly performed on all patients' BM, on PB of CAMT4, and on SF of CAMT2 with centromere-specific probes for chromosomes 7 (D7Z1), and 8 (D8Z2) (Cytocell Technologies, Cambridge, UK) either with single fluorochromes or in dual color combination. Nuclei from healthy subjects were used as control.

All the results are detailed in Table 1. The karyotype was consistently normal in patients CAMT1, CAMT3, and CAMT5, and parallel FISH analysis on interphase nuclei from BM confirmed the normal disomies 7 and 8. DEB test performed on PB of CAMT1, CAMT2, and CAMT3 excluded Fanconi anemia (FA).

Patient CAMT2 progressed to pancytopenia, with normal BM and PB karyotype, at the age of 30 months (January 2005), but in a subsequent analysis on BM, in May 2006, trisomy 8 was found in 1 mitosis out of 24 and 5 nuclei out of 616. Analysis on fibroblasts from a skin biopsy excluded a constitutional trisomy 8 mosaicism (Table 1). In patient CAMT4, the karyotype was normal in BM cells in 2001, at the age of 12 months, and in 2004 when progression to pancytopenia was observed, but in May 2006 a BM clone with monosomy 7 was found which persisted in the following analyses (Table 1).

A risk of evolution into myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) has often been assumed for CAMT, but in a search for *bona fide* CAMT patients who developed MDS/AML, we found only 3 such cases in the literature, and none of these was proved to carry mutations of the *MPL* gene: they are one refractory anemia with excess of blasts (RAEB) reported by King *et al*.,[2] and 2 cases mentioned by Alter,[6] a male with acute myelomonocytic leukemia (AMML) developed after an aplastic anemia phase, and a female with a pre-leukemic condition. These 2 latter cases were never reported in more detail, and were studied some decades ago.[6] In addition, a report is available of a CAMT patient with MPL mutations who developed a pre-B acute lymphoblastic leukemia.[7]

A review of CAMT cases with chromosome anomalies is even more difficult to carry out since cytogenetic results in the literature are often incorrectly mentioned, incomplete, and probably questionable. Among the patients with MDS/AML mentioned above, clonal chromosome changes in the BM were reported to be present in 2: the child with RAEB[2] with trisomy 21 in 10-15% of the cells, and the patient with AMML[6] with different anomalies of chromosome 19 (monosomy, trisomy, deletion) in 11 cells out of 55. As to CAMT without MDS/AML, King *et al*.[2] reported 2 patients with possible chromosome anomalies in PB, but the case identified as CAMT9 showed a translocation only in one cell out of 19, whereas CAMT13 showed a supernumerary marker (not better defined) in 94% of the cells. The only case from the literature with a reliable clonal anomaly in the BM was reported by Steele *et al*.,[8] who found monosomy 7 in 12 out of 20 mitoses and 91 out of 200 interphase nuclei. Mutations of the *MPL* gene were identified in these 3 patients.[4,8]

In our 5 patients, BM clonal anomalies were found in 2, in the absence of MDS/AML: one case of monosomy 7 and one of trisomy 8; the latter was demonstrated not to be a constitutional mosaicism, as is the case in 15-20% of patients with MDS/AML and trisomy 8.[9] While no exhaustive cytogenetic study on CAMT is available, our small group of patients was monitored over time for possible clonal chromosome anomalies in BM. We suggest that clonal chromosome changes are frequently acquired in the BM of CAMT patients: they often seem to be the most typical of MDS, monosomy 7 and trisomy 8. Interestingly, in both our patients the abnormal clones were found when the disease had already progressed to pancytopenia (Table 1), and the patient reported by Steele and co-workers showed monosomy 7 when CAMT had evolved to BM aplasia.[8]

In both our patients, the abnormal clone was detected not at the first chromosome analysis but after and showed a trend to expansion (Table 1). In particular, if we take into account evaluations by interphase FISH, in patient