

Background

Due to improved blood transfusion and chelation therapy, survival has been increased in thalassaemia patients with the consequence of complications like osteoporosis not seen during childhood and adolescence. The diagnosis of osteoporosis or osteopenia is assessed by endocrinological parameters and bone mineral density (BMD) measurements. The obvious shortcomings of conventional BMD methods like dual energy x-ray absorptiometry (DXA), can be overcome by simultaneously assessing the microarchitecture of the bone using high-resolution peripheral quantitative computed tomography (HR-pQCT).

Patients and Methods

In 18 regularly transfused patients (age: 13 - 43 y, 50% female) with beta-thalassaemia major (n = 11), -intermedia (n = 6), and CDA-II (n = 1), the planar BMD of lumbar spine (LS) and total hip was measured by DXA (Hologic QDR 1000+, Waltham, USA). Age related Z-scores were calculated from BMD. In addition, we assessed the volumetric BMD and the trabecular architecture of the non-dominant distal radius and tibia by HR-pQCT (XtremeCT®, SCANCO Medical AG, Bassersdorf, Schweiz). Liver iron concentration by SQUID biomagnetometry and endocrinological parameters were also determined. Normal values are adopted from Boutroy et al, 2005.



Measurement of volumetric bone mineral density and bone microarchitecture of a thalassaemia patient's radius by high-resolution peripheral quantitative computed tomography, HR-pQCT, (XtremeCT®: resolution 80 µm, total body equivalent radiation dose 3 µSv).

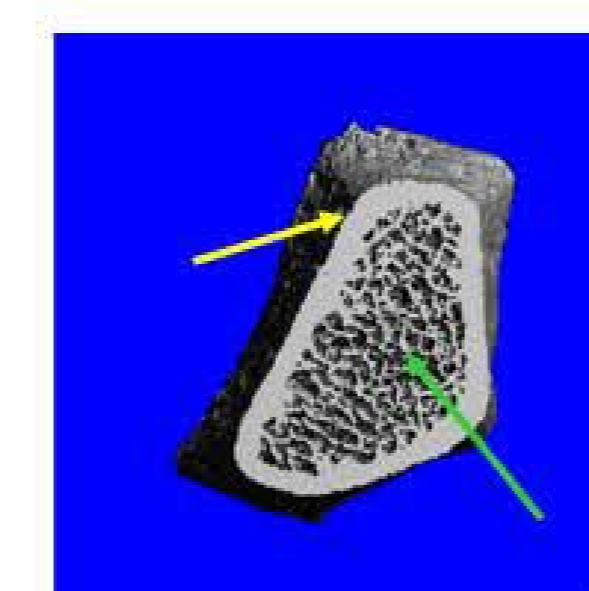
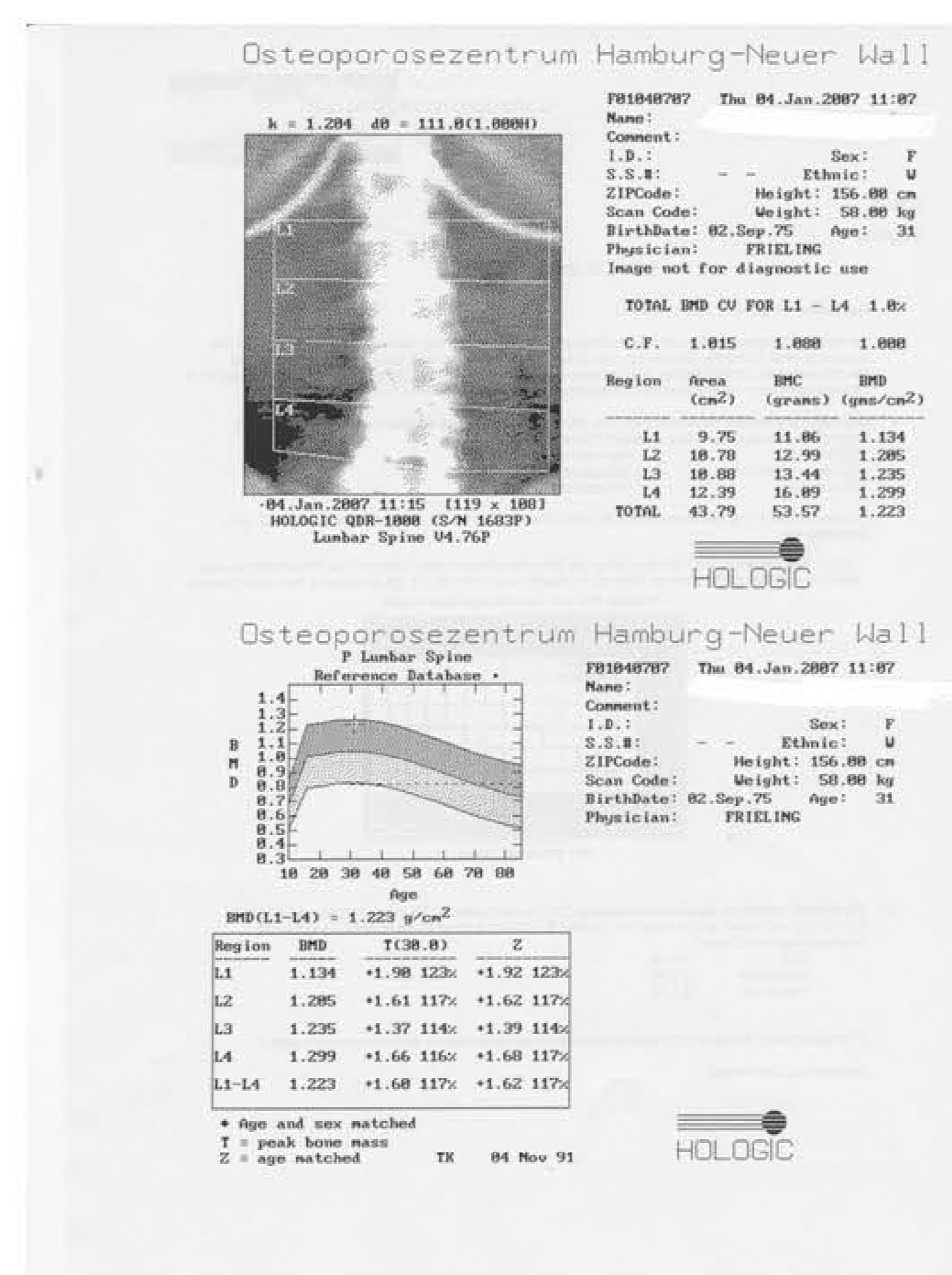
Results

In most patients low Z-scores (< -1.0) were measured by DXA (LS Z-score range: 1.6 to -3.530). Planar hip (DXA) correlated with total volumetric (HR-pQCT) bone densities of the radius (Spearman rank correlation coefficient $R_s = 0.66$, $p = 0.003$) and the tibia ($R_s = 0.63$, $p = 0.005$), in contrast to the planar BMD of the lumbar spine ($R_s = 0.52$ and 0.34 for the radius and tibia, respectively). Liver iron was mainly correlated with tibial TrabSp SD ($R_s = 0.54$, $p = 0.025$).

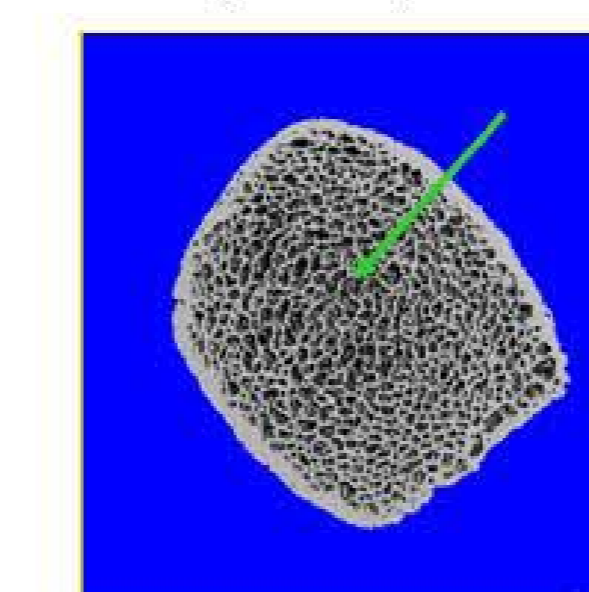
Patients with hypogonadism (n = 9) were significantly different from normals (range: 96-328 µm) with respect to radial TrabSp SD (range: 126-3642 µm, $p = 0.02$), but not to LS Z-score ($p = 0.4$). Their spongiosa was porous or nearly dissolved. Patients with fractures (n = 5) had lower total densities ($p = 0.02$) and trabecular TrabSp SD ($p = 0.02$) at the tibia and started blood transfusions (Tx-age) at a higher age ($p = 0.023$). However, Z-scores did not reflect the fracture risk in this patient group ($p = 0.1$).

Exemplarily, we show two female patients with and without hypogonadism measured by DXA and HR-pQCT:

Patient without hypogonadism (32 y, f, β-thalassaemia intermedia)

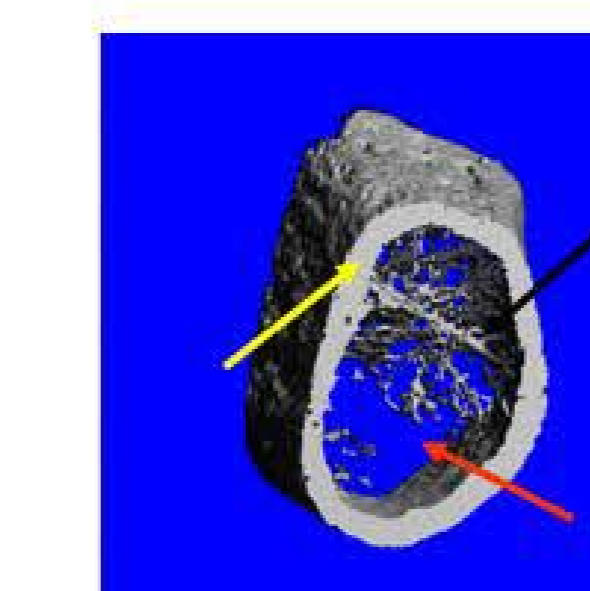
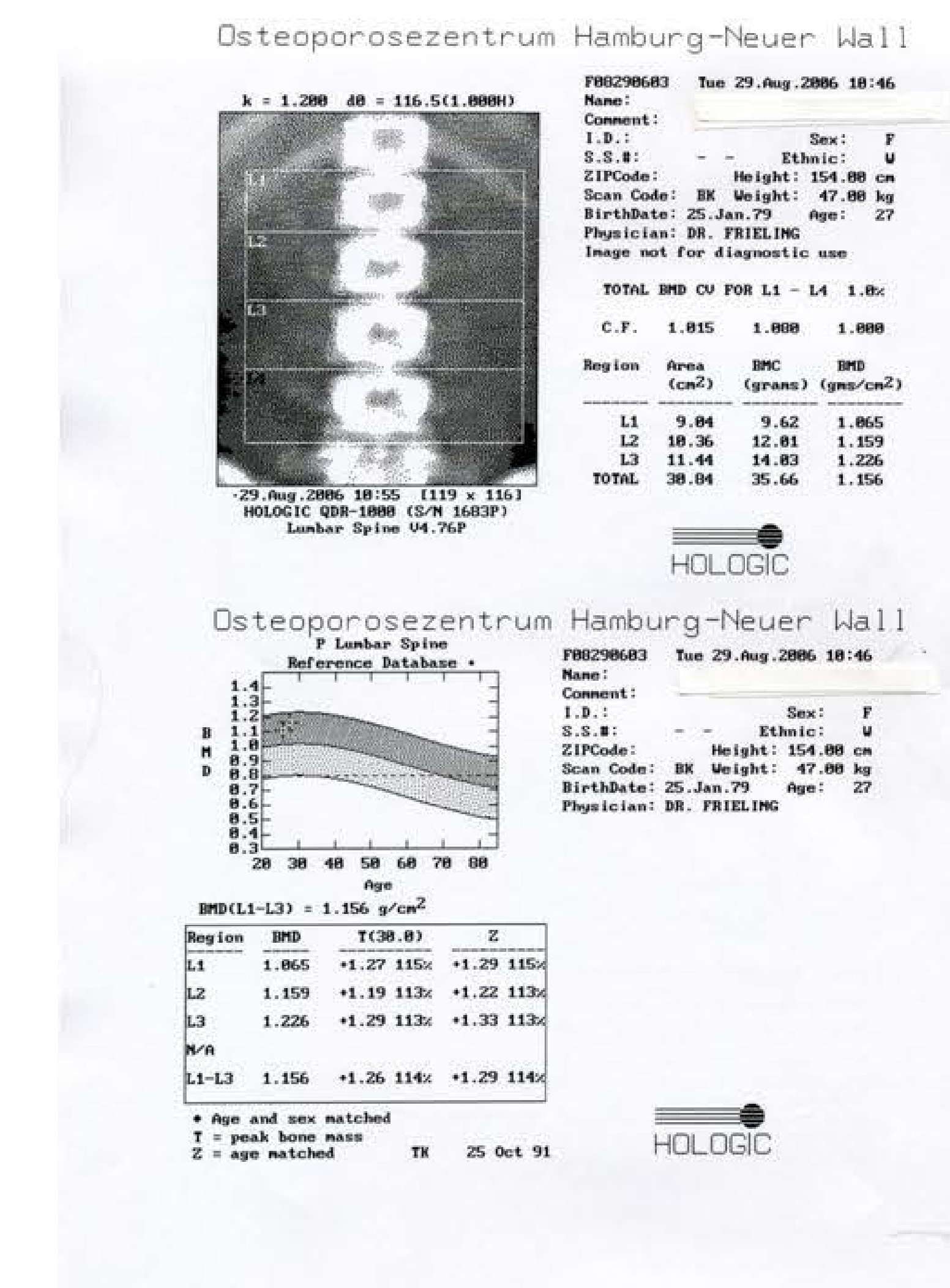


Proximal Radius
By HR-pQCT

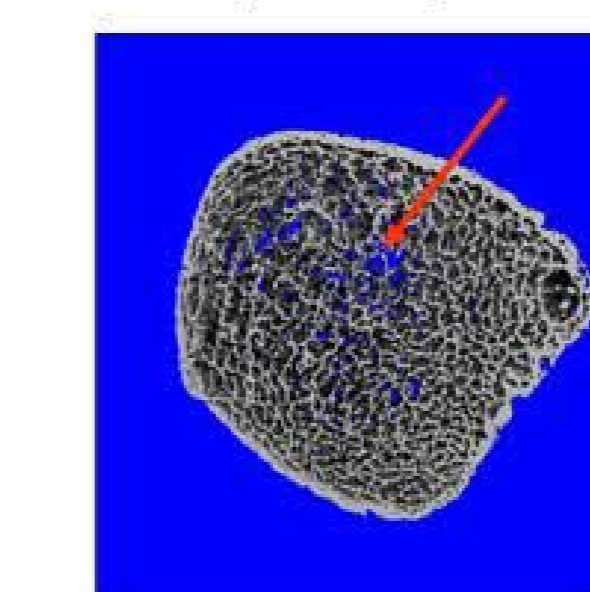


Distal Tibia

Patient with hypogonadism (27 y, f, β-thalassaemia major)



Proximal Radius
by HR-pQCT



Distal Tibia

The two patients have a strong cortical bone corresponding with their age (↑, 950 and 820 µm, normal: 506 – 1102 µm). The spongiosa at the radius of the patient at left (↑, trabecular inhomogeneity parameter TrabSp SD = 177 µm) is normal (96 – 328 µm), while the spongiosa of the patient with hypogonadism is nearly dissolved (↑, TrabSp SD = 1609 µm). This is more prominent at the radius than at the tibia (TrabSp SD = 190 and 496 µm). The relative thick trabecular bone (↑, right) might have been caused by displacement of the spongiosa by hyperplastic bone marrow.

Z-scores of lumbar spine by DXA measurements result in values of the upper normal range (1.62 and 1.29).

Summary

In diagnosing osteopenia or osteoporosis in patients with thalassaemia Z-scores seem to underestimate the fracture risk because a normal cortical thickness and density may conceal a porous trabecular structure. Endocrinological failures, especially hypogonadism, were responsible for the pathological microarchitecture of distal radius and tibia, while bone marrow expansion as in thalassaemia intermedia and liver iron concentration seem to play a minor role. These first results from bone microarchitecture measurements in thalassaemia have to be confirmed by larger patient numbers of different gender and age.