

# Quantitative and semiquantitative evaluation of Erythropoietin conditioned signal intensity-alterations in MRI of Femur in patients with cancer anaemia

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## Introduction

SI-alterations of the bone marrow of Femur are described in literature in a lot of malignant and non-malignant processes [3] and for the lumbar spine in combination with bone marrow –stimulating factors [1,4].

We are evaluating quantitatively and semiquantitatively SI alterations in MRI of femoral bone marrow in patients with cancer anaemia undergoing therapy with Erythropoietin or placebo.

## Methods

We examined 30 patients (15 Epoetin beta, 15 Placebo) of a randomised, double-blind multicenter trial with head and neck cancer patients, whose cancer anaemia was treated by Erythropoietin or placebo undergoing radiotherapy [2].

For the measurement of the Femur in a sagittal plane with a slice thickness of 4mm we used an 1.5 tesla tomograph (Magnetom Symphony, Siemens, Erlangen Germany) with the following echo sequences: T1 weighted SE, opposed-phased gradient echo, in-phased-opposed-phased subtraction and STIR. After selecting 5 regions of interest (ROI) in the Femur the signal intensities were registered quantitatively before the first application of the trial-substances, after reaching a determined haemoglobin-value (mean 48d;max 96d, min 10d) and after finishing the radiotherapy (mean 133d; max 253d, min 75d) and were standardised by a reference ROI in adductor muscle [1,4]. For the statistical evaluation of significant differences between the Erythropoietin beta- and the Placebo – group and within these groups we used independent / paired t-tests. The semiquantitative assessment was realised with blinded data by two independent radiologists. The quota of haematopoetic bone marrow in MRI of Femur was optically classified in low, nodular, scattered and uniform, the changes between times of measurement were classified in low increase, high increase, constant, low decrease and high decrease [3,1].

## Results

The quantitative evaluation of standardised SI-values showed statistically significant differences ( $p<0,05$ ) between the two trial-groups for the metaphysis of Femur in the T1 weighted SE-Sequence during the therapy with Erythropoietin. There was a SI-decrease of average 12% after 48d (mean) and after 133d (mean) with an increase of 10% nearly a return to the starting-value. In OPP and STIR-sequences we found significant and borderline significant ( $0,05>p<0,07$ ) differences between the times of measurement and between the two trial-groups for particular ROIs, but likewise within the placebo-group. For the semiquantitative evaluation we looked for SI-alterations between times of measurement (M) 1 to 2 and 1to 3 (Table 1).

EPO N=15	T1 M1-2	T1 M1-3	OPP M1-2	OPP M1-3	STIR M1-2	STIR M1-3
high decrease	<b>60%</b>	14%	34%	20%	0%	0%
low decrease	14%	34%	<b>47%</b>	<b>47%</b>	0%	0%
Constant	20%	<b>47%</b>	34%	34%	14%	<b>47%</b>
low increase	7%	7%	0%	0%	20%	27%
high increase	0%	0%	0%	0%	<b>67%</b>	27%

Placebo N=15	T1 M1-2	T1 M1-3	OPP M1-2	OPP M1-3	STIR M1-2	STIR M1-3
high decrease	0%	0%	7%	0%	0%	0%
low decrease	14%	7%	7%	7%	0%	0%
constant	<b>87%</b>	<b>93%</b>	<b>87%</b>	<b>87%</b>	<b>87%</b>	<b>87%</b>
low increase	0%	0%	0%	0%	7%	7%
high increase	0%	0%	0%	0%	7%	7%

Table 1: Results of semiquantitative evaluation

## Discussion

The increase of haematopoiesis after treatment with Erythropoietin appears in the metaphysis of Femur in the T1 weighted SE-sequence as a significant decrease of the standardised SI that shows the change from yellow to red bone marrow. Using the semiquantitative evaluation method, we find significant changes as well in the OPP as the STIR-sequence. The quantitative evaluation is a method with a very high sensitivity for changes in bone marrow areas, defined by placing the different ROIs [4]. In the OPP- and STIR-sequence we cannot demonstrate a continuous, statistically proven difference between the times of measurement and between the trial groups, because we found differences at measure time 1 (before application) and differences within the placebo group. All examined patients suffered from head and neck cancer and a cancer anaemia, some have a smoking anamnesis, some were given an iron substitution. These are factors, which could explain changes within the femoral bone marrow without connection to Erythropoietin. Further studies with a higher number of patients should investigate the SI-changes in femoral bone marrow compared with a healthy control-group.

## References

1. Althoefer C et al., J Magn Reson Imaging 2001, 14, 141-46
2. Henke M et al., Lancet 2003, 362, 1255-60
3. Tsunoda S et al., Blood 1997,89, 286-90
4. Ghanem N et al., Proc Intl Soc Mag Reso Med 2002,10

Fig. A: T1 weighted SE-sequence, time of measurement 1-3, of a Erythropoietin patient (top) and a placebo patient (bottom).

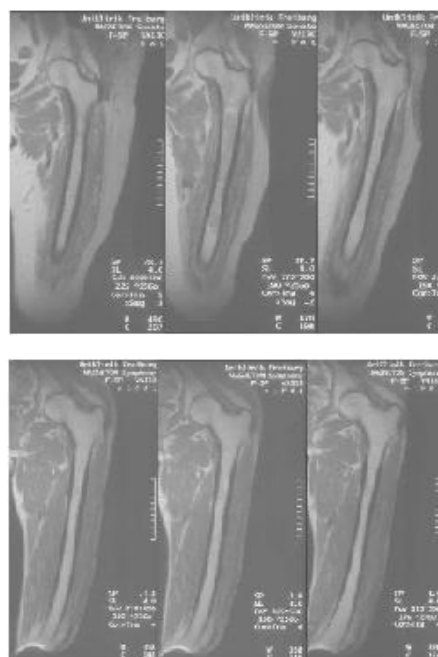


Fig.A: T1 weighted SE-sequence, 3 measure times, of a Erythropoietin patient (left) and a placebo-patient (right)