Magnetic resonance imaging (MRI) and image analysis of post-radiation changes in patients with bone metastases

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Authors: E. Solomou¹, O. Romanos¹, P. Georgiadis¹, D. Kardamakis¹, D. SIABLIS²; ¹Patras/GR, ²RIO PATRAS/GR
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Purpose

Aim of the present study was the evaluation of post-radiation lesions with MRI and image analysis, in patients with bone metastases undergoing radiation therapy.

The skeletal system is the 3rd commonest site for localization of metastasis, after liver and lung. Nearly 70% of patients with cancer will at sometime present bone metastases, where most of them will be under palliative radiation therapy (RT) [1].

For many decades, RT has been established successfully as a treatment method for the management of metastatic bone disease, bringing considerable pain response and a reduction in complication rates [2].

Magnetic Resonance Imaging (MRI) is the method of choice (as a non invasive method) to detect not only skeletal metastases, but also to evaluate post radiation changes in bone marrow (BM), as it provides information at the level of cellular and chemical composition [3].

Up to date, there are many references to the literature concerning the post radiation changes with MRI within and besides the fields of the irradiated area [4].

This paper focuses on the post-radiation changes detected with MRI and compares them with an automated classification system, in order to determine better the presence of early post radiation alterations.
Methods and Materials

35 patients with bone metastases have been studied since June 2008. All patients had presented osseous metastases from various primary malignancies.

- Inclusion criteria were: (a) histologically confirmed solid tumors and (b) bone metastases, confirmed by X-ray, CT, MRI, or bone scintigraphy.
- Patients with a known history of blood or hematopoietic disease, a pathologic fracture, epidural spinal cord compression, hypercalcemia, hypocalcemia, Paget’s disease, primary hyperparathyroidism, or patients with previous radiotherapy to the affected region were excluded.

All patients received external-beam radiotherapy with a 6-MV linear accelerator to the specified treatment site. The total dose administered at tumor depth ranged from 30 to 40 Gy, with a daily dose of 1.8 - 2.0 Gy.

MRI was performed in a 1T scanner at the beginning of radiotherapy and 12 - 18 days later. T1-SE, T2-TSE and fat-suppression sequences were used. Visual changes of tissue alterations were observed in post radiation MR images relative to pre-irradiation MR aspect [5]. Areas of interest were selected and quantitative measurements were evaluated by the method of Region of Interest (ROI). Each measurement was repeated 3 times for the intra-observer variation analysis as well as the calculation of the mean values [6].

Additionally, 1st and 2nd order textural features were extracted from these images and were introduced into a probabilistic neural network classifier (PNN) in order to create an automated classification system for those lesions. From each ROI, a series of 36 features were extracted (Table 1) All features were normalized to zero mean and unit standard deviation [7].

**Table 1. Textural features extracted.**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histogram (1st order statistics)</td>
<td>Mean Value, Standard Deviation, Skewness, Kurtosis</td>
</tr>
<tr>
<td>Mean and range of 0°, 45°, 90° and 135° co-occurrence matrices (2nd order statistics)</td>
<td>Angular Second Moment, Contrast, Correlation, Sum Of Squares, Inverse Difference Moment, Sum Average, Sum Variance, Sum Entropy, Entropy, Difference Variance, Difference Entropy</td>
</tr>
</tbody>
</table>
Mean and range of 0°, 45°, 90° and 135° run-length matrices (2nd order statistics) Short Run Emphasis, Long Run Emphasis, Gray Level Non Uniformity, Run Length Non Uniformity, Run Percentage

Two Least Square Features Transformation Probabilistic Neural Network (LSFT-PNN) based classification systems were designed to discriminate:

- (a) between pre-radiation and post-radiation lesions and
- (b) between the post-radiation lesions (oedema, fatty conversion and hemorrhage). Fig. 1 on page 5

To combine the diagnostic information encapsulated in the MR images acquired with all three MR series (T1-SE, T2-TSE and STIR), a multi-series classification procedure was utilized. Fig. 2 on page 5

Accordingly, each ROI from each MR series was classified in a separate LSFT-PNN classifier. Finally, the output of each classifier was used in the formulation of a collective decision using the majority vote rule [7].

The whole design and evaluation procedure was repeated ten times and the classification results where averaged. Apart from the linear (1st degree), the quadratic (2nd degree) LSFT procedure was also employed to investigate the classification accuracy behavior of the LSFT-PNN classifier as higher-degree non-linear elements were introduced in its discriminant function.
**Fig. 1:** Classification system designed to discriminate between the post-radiation lesions.

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**Fig. 2:** Multi-Series Classification Procedure.

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Results

Changes of signal intensity in T1, T2 and fat suppression sequences were evaluated for the presence of oedema, fatty conversion of the bone marrow and haemorrhage, within the limits of the irradiated area. Fig. 3 on page 9 Fig. 4 on page 9

The best overall classification accuracy of the system designed to discriminate between pre-radiation and post-radiation lesions was 93.02% employing the LSFT-PNN multi-sequence classification scheme and the ECV method (Table 2). Individual accuracies in discriminating between pre-radiation and post-radiation lesions were 90.91% and 95.24% respectively.

Best feature vector, used for the optimal design of the classification scheme, comprised four textural features;

- the skewness,
- the difference entropy,
- the sum average and
- the sum entropy.

Employing the LSFT-PNN multi-sequence classification scheme and the ECV technique, the discrimination accuracy of the classification system designed to distinguish between the three types of post-radiation lesions (edema, fatty conversion and hemorrhage) was 86.67% (Table 2).

The best feature vector, employed for the optimal design of the classification scheme, comprised five textural features;

- the standard deviation,
- the difference entropy,
- the sum average,
- the entropy and
- the long run emphasis.

Table 2. Classification results utilizing the ECV method and the LSFT-PNN multi-sequence classification scheme (average after ten ECV repetitions).

<table>
<thead>
<tr>
<th>Number of Features</th>
<th>Pre-Radiation Vs Post-Radiation</th>
<th>Oedema Vs Fatty Conversion</th>
<th>Oedema Vs Hemorrhage</th>
<th>Overall Accuracy (%)</th>
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<tbody>
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<td>Overall Accuracy</td>
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<td>Overall Accuracy (%)</td>
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<td><strong>86,67</strong></td>
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Fig. 3: T1-SE images, in a patient presented with metastases in the lumbar spine: (a) Before RT.

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Fig. 4: T1-SE images, in a patient presented with metastases in the lumbar spine: (b) 18 days after the beginning of RT.

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Conclusion

MR signal changes of the bone marrow during and after irradiation are considered to be time and dose dependent. Location and extend of the affected anatomical area, the age of the patient, as well as additional chemotherapy also affect these alterations.

The role of MRI as a method of choice for the early detection and characterization of bone marrow post-therapeutic changes has been well established. Several studies have shown that shortly after the start of radiation therapy the bone marrow becomes hypocellular, its vascular architecture gets destructed and fatty marrow progressively replaces the hematopoietic marrow [8,9].

Because of these alterations, high signal intensity is produced in T1-SE images. During the first weeks after the initiation of radiation therapy, areas of increased signal intensity in STIR images may represent edema, hemorrhage or an early reflux of non irradiated cells. There has been controversy over the exact time when edema, hemorrhage and fatty degeneration appear and disappear [10].

In this study, we focused on these early post radiation effects on the bone marrow. We used the information provided by conventional MR imaging in combination with an automated classification system in order to improve the detection and characterization of bone marrow alterations. This classification system gave us the opportunity to determine and characterize precisely even the smallest lesions in the bone marrow which are not really obvious by other radiological methods.
References


Personal Information

Ekaterini Solomou, Assistant Professor of Radiology. MRI Unit, Department of Radiology, University Hospital of Patras, Rio-Patras, Greece

solomoua@upatras.gr

Odyssefs Romanos, MD. formerly: Resident in Radiology, Department of Radiology, University Hospital of Patras, Rio-Patras, Greece; currently: Trust Fellow in Radiology, Department of Radiology, King's College Hospital, London, UK

odyroman@yahoo.gr

Pantelis Georgiadis, PhD. Biomedical Engineer, MRI Unit, Department of Radiology, University Hospital of Patras, Rio-Patras, Greece

pantelisgeorgiadis@gmail.com

Dimitrios Kardamakis, Professor of Radiation Oncology. Department of Radiology, University Hospital of Patras, Rio-Patras, Greece

kardim@upatras.gr

Dimitrios Siablis, Professor of Radiology. MRI Unit, Department of Radiology, University Hospital of Patras, Rio-Patras, Greece

siablis@upatras.gr