Mean curve analysis of pattern of enhancement of various bone tumors on high resolution dynamic contrast enhanced MR and its role in characterizing various bone tumors

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Aims and objectives

To analyze the pattern of mean time intensity curve and enhancement characteristics of various bone tumours on dynamic contrast enhanced MR (DCE-MRI).

To study its role in differentiating benign from malignant aetiologies and in further characterizing various specific lesions.
Methods and materials

BACKGROUND

Though DCE-MRI has been around for many years, its role in imaging and characterisation of bone tumors has been especially unexplored.

Conventional contrast enhanced studies are based on the display of a single snapshot of tumor enhancement after contrast administration and though the anatomical information derived from such images is valuable, functional information is lacking[1]. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI), on the other hand relies on fast and ultrafast acquisition of a series of MRI images before, during and after the administration of a gadolinium (Gd) based contrast agent, so that the variation of MR signal intensity with time can be recorded and a sequential set of morphological data is collected. DCE-MRI enables the depiction of physiologic alterations as well as morphologic changes[1].

Variations in microvascular structure and pathophysiology give rise to temporospatial variations in the enhancement patterns that can provide valuable information on tumor characteristics. DC enhancement patterns depend on physiological factors like vessel density, blood flow, endothelial permeability and the size of the extravascular extracellular space in which the contrast is distributed[2].

During DCE-MRI, tumors demonstrate rapid early enhancement followed by plateauing or mild washout compared to normal tissue[3]. This is due to the neoangiogenesis that occurs especially in malignant tumors. There is increased contrast uptake in the early phase due to increased vessels followed by plateauing due to contrast pooling in the neovasculature and surrounding interstitium of the tumor due to altered endothelial permeability. In cases of infection and inflammation, the increased enhancement is predominantly due to vasodilation that occurs due to the recruitment of various inflammatory molecules and so the pattern is of gradual progressive enhancement. Benign but highly vascular tumors show a pattern of enhancement that simulates the surrounding normal vessels, i.e. rapid uptake with wash out as seen in osteoid osteoma[4] and giant cell tumors.

DCE-MRI is a feasible alternative for non-invasive evaluation of tissue microvasculature in vivo.
It also differentiates reactive edema from viable tumor, as viable tumor enhances in the early phase while reactive edema enhances late. DCE-MRI also has the added advantage of capturing the arterial and the venous phases separately which is sometimes of great help in delineating the vascular supply to a tumor, useful information to the operating surgeons.

**METHOD AND MATERIALS**

77 patients with bone lesions detected on radiographs were included.

The study was performed on either a 1.5 or a 3T magnet. After completing the preliminary plain MRI with the standard protocol that included coronal, sagittal and axial T1W, T2W and STIR sequences, DCE-MRI was performed. Conventional post contrast FS T1W images in all three planes were also obtained following the dynamic studies.

The IV contrast agent used was Magnavist (Gadopenteate dimeglumine). Contrast injection was performed through the antecubital vein using an automated pressure injector system. A single dose of contrast (0.2 mmol/kg) of standard gadolinium chelate was administered at a rate in the region of 3.5 ml/sec. Contrast injection rate was calculated so that the overall period of administration was kept constant between patients. This was followed by a chaser injection of approximately 20-30 ml of normal saline given at the same rate as the contrast. This is essential to empty the draining veins and to ensure that the contrast enters the systemic circulation as a coherent bolus.

The right antecubital vein was preferred as variations in jugular venous anatomy on the left sometimes may lead to jugular reflux impairing the coherence of contrast bolus\[2\].

The dynamic study was performed in a plane that not only showed the pathology best but also displayed normal surrounding tissue and a large blood vessel which was essential to analyse the dynamics of the tumor in relation to the contrast concentration changes in the plasma and the surrounding normal tissue over time.

DCE-MRI was performed using a T1 TSE 3D sequence with fat suppression with 80-100 slices per slab, a flip angle of 25 or 10 degree, TR/TE of 3.4/1.3 ms and recon matrix of 127X256 or 152X106. 15 serial image sets were obtained at a temporal resolution of 15-16 sec over 4-5 minutes post injection.
A region of interest (ROI) within the tumor tissue was then appropriately selected, such that it contained only the enhancing solid component and did not include the necrotic component or surrounding normal tissue.

A mean time intensity curve of the lesion ROI was then obtained from the DCE-FST1W images. The curve was classified into one of the five types -

- Type 1 Fig. 1 on page 6 - rapid uptake with washout,
- Type 2 Fig. 2 on page 6 - rapid uptake with plateauing,
- Type 3 Fig. 3 on page 7 - gradually progressive,
- Type 4 Fig. 4 on page 8 - moderate uptake with plateauing and
- Type 5 Fig. 5 on page 9 - moderate uptake with washout.

The lesions showing delayed enhancement were put in a separate category.

Final diagnosis was established by histopathology, imaging follow up and response to RFA in cases of osteoid osteoma.
Images for this section:

Fig. 1: Type 1 curve: Rapid uptake with washout in a 18 yr old lady with osteoid osteoma of the distal tibial metaphyseal cortex.

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Fig. 2: Type 2 curve: Rapid uptake with plateauing in a 21 y old man with recurrent giant cell tumor.

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Fig. 3: Type 3 curve: gradually progressive pattern of enhancement in a 20 yr old lady with tibial osteomyelitis.

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Fig. 4: Type 4 curve: Moderate uptake with plateauing in a 24 y man with biopsy proven osteosarcoma.

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Fig. 5: Type 5 curve: Moderate uptake with washout in a clavicular metastases in a 47 yr old known case of ca lung.

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Results

41 out of 77 patients had malignant tumors which included osteosarcoma, Ewing's sarcoma, chondrosarcoma and metastases. 38 of these 41 tumors showed either a type 4 or 5 curve. Fig. 6 on page 13 Fig. 7 on page 13 Fig. 8 on page 14 Fig. 9 on page 14

The 36 cases of benign bone lesions included osteomyelitis, osteoid osteoma, fibrous dysplasia, osteoblastoma, chondromyxoid fibroma, vascular malformation, aneurysmal bone cyst, non-ossifying fibroma, simple bone cyst, giant cell tumor and enchondroma. Cases of fibrous dysplasia with secondary ABC transformation and of liposclerosing myxofibromatous tumor were included as well. Most of these tumors either showed a type 3 curve or mild delayed enhancement, with the characteristic type 1 and 2 curves shown by highly vascular tumors like osteoid osteoma, giant cell tumors and ABC.

Osteomyelitis, a great tumor mimic showed a characteristic gradual progressive pattern of enhancement, a type 3 curve. Fig. 10 on page 15 Fig. 11 on page 16

Fibrous tumors like fibrous dysplasia, chondromyxoid fibroma showed delayed or no enhancement patterns. Fig. 12 on page 17 Fig. 13 on page 18

The characteristic arterial phase enhancement of the nidus was found to be highly specific as well as sensitive for osteoid osteoma. [4] Fig. 14 on page 19

CT scan, earlier considered the most specific for detecting the nidus of osteoid osteoma, failed to do so in two of the 7 cases of osteoid osteoma (of the total 15 cases of osteoid osteoma imaged on MRI) where a CT scan was performed. One was diagnosed as a focal cortical defect and the other as osteomyelitis on CT scan. In both these cases, the nidus was characteristically seen on the arterial phase of the DCE-MRI. Fig. 15 on page 19 Fig. 16 on page 20 Fig. 18 on page 22

Certain lesions which very closely mimic osteoid osteoma based on both location and radiological appearance, could also be easily distinguished with DCE-MRI. One such case was of a young 14 y old girl with pain in the knee especially aggravated at night. Based on CT scan and conventional MRI done elsewhere, a diagnosis of osteoid osteoma was made. However, DCE-MRI failed to reveal the characteristic arterial enhancing nidus and a diagnosis of focal epiphyseal osteomyelitis was made. Fig. 19 on page 23 Fig. 20 on page 23. The child was started on antibiotics to which she showed dramatic response with significant regression of the lesion on follow up after 4 weeks. Thus,
the child was saved from unnecessary intervention that would have followed the wrong diagnosis of osteoid osteoma.

DCE-MRI also plays a role in detecting residual disease/recurrence in treated cases of osteoid osteoma where the altered bone architecture post treatment may preclude the confident visualisation of a new nidus within or next to the treated osteoid osteoma[5] Fig. 20 on page 23 Fig. 21 on page 24.
Fig. 6: Precontrast T1W and post contrast FS T1W coronal images show a heterogenously enhancing aggressive lesion involving the distal femoral epimetadiaphysis, in a 24 y man with biopsy proven osteosarcoma.

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Fig. 7: Mean curve analysis of the same patient showed a type 4 curve.

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Fig. 8: Pre contrast T2,T1 and post contrast FS T1W coronal images of the shoulder in a case of Ca lung show an aggressive metastatic lesion involving the distal clavicle.

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Fig. 9: The mean curve analysis shows a type 5 curve.
Fig. 10: STIR, T2, T1 and post contrast FS T1W coronal images of the tibia show an aggressive osteolytic lesion. Mean time intensity curve showed gradually progressive enhancement (type 3) and a diagnosis of osteomyelitis was given and also proved on the subsequent biopsy.

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Fig. 11: Mean curve of the patient above with characteristic type 3 curve, suggestive of benign nature of the lesion.

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Fig. 12: Axial T2, T1 and post contrast FS T1W images show an expansile heterogenously enhancing lesion involving the medial cortex of proximal fibular diaphysis.

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Fig. 13: Mean curve analysis shows minimal or no enhancement in the early phases with the enhancement seen only on the delayed single snapshot T1FS images obtained at the end of the DCEMR study.
Fig. 14: Axial T2,T1W images show cortical irregularity involving the lateral aspect of the distal tibial metaphyseal cortex with subjacent marrow edema. The single snap shot post contrast FST1 images do not add much to the information. The arterial phase captured on the dynamic studies shows the characteristic enhancing nidus, confirming the diagnosis of osteoid osteoma.
Fig. 15: The axial and coronal reconstructed CT scans show a well-defined focal osteolytic lesion involving the medial cortex of the distal femoral metaphysis, mimicking a fibrous cortical defect. No nidus was seen.

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Fig. 16: The coronal STIR MRI image shows marrow edema surrounding the lesion.

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**Fig. 17:** The axial DCE MR in the arterial phase clearly shows the nidus, thereby confirming the diagnosis of osteoid osteoma as against the diagnosis of fibrous cortical defect on CT scan.

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**Fig. 18:** Axial T2, T1 and post contrast FS T1W images show a well defined osteolytic focus in the proximal tibial epiphysis with extensive surrounding edema mimicking osteoid osteoma. However an arterial enhancing nidus was not seen on DCE MR studies and a diagnosis of focal epiphyseal osteomyelitis was given.

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**Fig. 19:** Follow up scan after 4 weeks of antibiotics show regression of the lesion, confirming the diagnosis of osteomyelitis.

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Fig. 20: 14 y old girl with recurrent pain in the left thigh following radiofrequency ablation of a femoral osteoid osteoma. MR performed for evaluation of cause of pain showed a focal lesion in the femoral diaphysis at the site of previous osteoid osteoma, with extensive surrounding marrow edema. There was a diagnostic dilemma of recurrence vs focal osteomyelitis and the single snap shot post contrast images were not of much help in differentiation.

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**Fig. 21:** The mean curve obtained on the DCEMR study revealed the characteristic type 1 curve with an arterial enhancing nidus, thereby confirming the diagnosis of recurrence and a repeat RFA was done.

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Conclusion

CONCLUSION

Analysis of the mean time intensity curve obtained with DCE-MRI has great potential in differentiating benign from malignant lesions which is especially useful in post-operative cases to distinguish recurrence from post-operative infection/inflammation. DCE-MRI plays an important role in the confirmation of the diagnosis of osteoid osteoma.

CLINICAL RELEVANCE/APPLICATION

Conventional single snapshot post-contrast imaging provides details only regarding anatomy and to a certain extent the composition of the tumor, as against DCE-MRI, which helps us understand the functional characteristics of various tumors and thereby further increase our level of confidence in differentiating benign from malignant tumors and also in further characterizing various tumors by analyzing their functional characteristics.

DCE-MRI can be easily incorporated into daily practice in all protocols where contrast is given for focal lesions, with no significant increase in the time required for the study. Most modern scanners have all the sequences required to perform DCE-MRI along with workstations and softwares for analyzing the data. Essentially, whenever contrast is given for a focal bone or soft tissue lesion, a DCE-MRI post-contrast protocol must be followed, given the lack of downside and the potential upside.
References


