

## Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) for the prediction of non-union consolidation



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### ABSTRACT

**Introduction:** Non-union perfusion can be visualized with dynamic contrast-enhanced (DCE) MRI. This study evaluated DCE-MRI to predict non-union consolidation after surgery and detect factors that affect bone healing.

**Materials and methods:** Between 2010 and 2015 non-union perfusion was prospectively quantified in 205 patients (mean age, 51.5 years, 129 men, 76 women) before intervention and at 6, 12, 26, 52 and more weeks follow-up. DCE-MRI results were related to the osseous consolidation, the ability to predict successful outcome was estimated by ROC analysis. The relevance of the body mass index (BMI) and the non-union severity score (NUSS) to the healing process was assessed.

**Results:** Tibial (n = 99) and femoral (n = 76) non-unions were most common. Consolidation could be assessed in 169 patients, of these 103 (61%) showed eventual healing and demonstrated higher perfusion than in failed consolidation at 6 (p = 0.0226), 12 (p = 0.0252) and 26 (p = 0.0088) weeks follow-up. DCE-MRI at 26 weeks follow-up predicted non-union consolidation with a sensitivity of 75% and a specificity of 87% (false classification rate 19%). Higher BMI (p = 0.041) and NUSS (p < 0.0001) were associated with treatment failure.

**Conclusions:** DCE-MRI perfusion analysis after non-union surgery predicts successful outcome and could facilitate the decision of early intervention. NUSS and BMI are important prognostic factors concerning consolidation.

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### Introduction

Fracture non-unions occur in 5–15% of all fractures depending on the fracture localization, soft tissue damage and contamination [1]. Research of bone regeneration and the treatment concepts of non-unions have progressed within the last years. The diamond bone concept [2,3] describes the most important factors in bone regeneration: the presence of osteogenic cells and growth factors, osteoconductive scaffolds and mechanical stability. Thus, in addition to traditional treatments like Ilizarovs external fixator [4,5], operative strategies like a two-step procedure according to Masquelet [6] or induced membrane technique and the use of bone

morphogenetic proteins (BMP 2 and 7) as growth factors [7,8] have been developed. Nevertheless, the correct diagnosis and treatment of failed bone regeneration is demanding [9].

Previous efforts focused on the clinical classification of non-unions (Non-Union Severity Score, NUSS) to standardize their treatment [10]. In the evaluation of osseous perfusion and successful non-union surgery, the dynamic contrast-enhanced MRI (DCE-MRI) is gaining more importance next to approved modalities such as conventional x-rays and computed tomography (CT). In a pilot study [11] DCE-MRI was feasible to assess vascularity within the non-union cleft, which is one of the principal elements of the diamond bone concept.

After non-union revision surgery, osseous consolidation is monitored with common clinical and radiologic examinations (x-rays, CT) whereas the overall healing time of non-unions shows great variety [12,13]. Therapy failure includes delayed consolidation and continuous instability. Until present, there are no set guidelines as to when revision surgery is indicated to promote

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consolidation [14,15] and only few studies are available that included not more than 100 individuals.

Thus, the aim of this prospective study on a large cohort was to evaluate the ability of DCE-MRI (index test) to predict non-union consolidation at an early stage after revision surgery and to detect additional factors that could affect bone healing. Consequently, failed non-union healing could be assessed earlier and patients referred to further therapeutic interventions such as additional bone grafting or implant change.

## Materials and methods

### Patient population and clinical assessment

Between 12/2010 and 03/2015 we prospectively included 225 patients that received non-union treatment at our university hospital. The study was conducted in accordance with the declaration of Helsinki and was approved by the local ethics committee (S-380/2010). All individuals accorded with the study protocol, gave their written informed consent and were examined by a senior trauma surgeon (CF). All received X-ray examinations

and standardized operative treatment according to the diamond bone concept.

Exclusion criteria were known intolerance of the contrast agent Dotarem® (n=8), cardiac pacemakers (n=6), cochlear implants, limited renal clearance, pregnancy, age under 18 years, excessive movement during the scan (n=3) or severe susceptibility artifacts without visible non-union (n=3) (Fig. 1).

Clinical and DCE-MRI examinations were performed preoperatively and, if possible, at 6, 12, 26 and at least 52 weeks after revision surgery. Non-union consolidation was defined as a successful clinical outcome including mechanical stability, i.e. ability to bear full weight, and radiologic signs of consolidation which were evaluated by a senior trauma and orthopedic surgeon (CF) as well as a senior musculoskeletal radiologist (MAW). Plain X-rays often feign consolidation despite a persisting non-union. Therefore, CT criteria of non-union consolidation were used according to previous recommendations [15–17]: at least 25% of the non-union gap area filled with newly formed bridging trabecula and/or at least 25% of the non-union area filled with newly formed cortical bridges across the fracture gap. Patients with non-unions that did not meet these aforementioned criteria

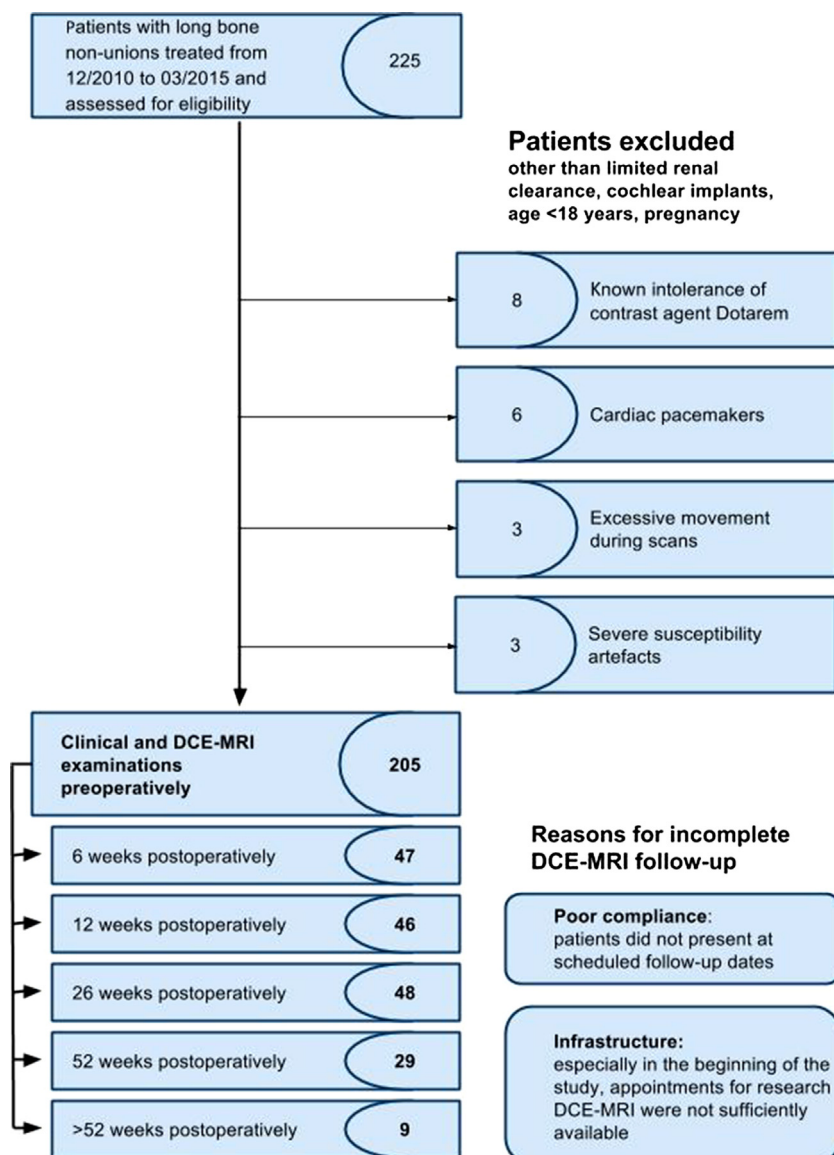


Fig. 1. Flowchart of patient recruitment and DCE-MRI examinations.

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