Treatment of osteochondral defects of the talus

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Chapter 17

General discussion
Chapter 17

General introduction

Osteochondral defects (OCDs) of the talar dome can be a disabling disorder that seriously affects the quality of life. Symptomatic OCDs pose a therapeutic challenge to the orthopaedic surgeon. Numerous treatment methods are available, each with advantages and disadvantages. This thesis aimed to evaluate and improve the current primary surgical treatment and to investigate alternative treatment methods.

Part I – Current concepts

Part I of the thesis reviewed the literature, presented a treatment algorithm, and discussed the use of arthroscopic ankle surgery. This part formed the basis for the remainder of the thesis. The review identified arthroscopic debridement and bone marrow stimulation as the primary surgical treatment of defects up to 15 mm. Osteochondral autograft transfer (OATS) and autologous chondrocyte implantation (ACI), with or without a cancellous bone graft, were recommended for secondary cases as well as large lesions.

The development of future treatment modalities described in chapter 2 included matrix-induced ACI, bone marrow-derived mesenchymal stem cells, biodegradable composite implants, correction osteotomy in the event of malalignment, metal resurfacing implants, demineralized bone matrix (DBM), and pulsed electromagnetic fields (PEMF). Some of these developments have become true options since the publication of the chapter. Different types of matrix-induced ACI have been reported in case series with two to 46 patients and a maximum follow-up of 3 years. The overall success rate was 90% but a comparison between the studies was unreliable due to differences in indications, techniques, and outcome measures. Furthermore, the analyses included duplicate follow-up publications from the same author. Bone marrow-derived cell transplantation loaded on a scaffold has been investigated in a series of 49 patients with a mean follow-up of 4 years. Although the mean American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score improved from 64 ± 14 preoperatively to 82 ± 17 at the final follow-up, a significant decrease was evident between 2 and 4 years. This investigation thus showed promising results but questioned the durability of the technique. Biodegradable composite implants have the advantages of a combined repair of cartilage and subchondral bone without the risk of donor site morbidity. However, after the report of four initial failures of commercially available composite implants, the procedure has been abandoned and scientific progress of this technique has decreased. Correction osteotomy for OCDs in malaligned ankles seems a promising solution but clinical results of this procedure are not yet available. The applicability of metal resurfacing implants, DBM, and PEMF was investigated in this thesis.

Part II – Primary arthroscopic debridement and bone marrow stimulation

Most OCDs can be treated by an anterior arthroscopic approach with the ankle in full plantar flexion. In case of posterior OCDs, it is challenging to treat the defect with this technique, since the ankle is a congruent joint with limited surgical access to the posterior talar surface. A posterior OCD can be approached with a two-portal hindfoot technique developed by van Dijk. The purpose of chapter 4 was to assess whether preoperative computed tomography (CT) of the ankle joint in full plantar flexion
was able to predict the anterior arthroscopic accessibility of talar OCDs. The study showed that measurements on CT scans of the ankle in full plantar flexion were a reliable and accurate preoperative method to determine the in situ arthroscopic location of talar OCDs. The findings of chapter 4 were followed by the study presented in chapter 5. The dual purpose of the study described in this chapter was (1) to quantify the anterior arthroscopic reach of the talus (i.e., proportion of the talar dome anterior to the anterior distal tibial rim) with the ankle in full plantar flexion, and (2) to identify predictive factors of the arthroscopic reach. The following conclusions were drawn: (1) almost half of the talar dome is accessible anterior to the anterior distal tibial rim, and (2) the clinical plantar flexion angle is an independent predictive factor of the arthroscopic reach of both the medial and lateral talar dome.

This study was the first to quantify the arthroscopic reach of the talus in a representative patient population. Previously, cadaveric studies investigated exposure of the talus with different open surgical approaches.\(^{293,456}\) Muir et al. compared seven open approaches in nine cadaver specimens.\(^{293}\) An anteromedial arthrotomy provided a mean access of 47\% (range, 41\% – 60\%) of the medial talar dome in the sagittal plane. An anterolateral arthrotomy provided 43\% (range, 37\% – 50\%) sagittal access of the lateral talar dome. Young et al. found that a median of 50\% (range, 44\% – 58\%) of the anteroposterior medial talar dome length could be reached through an anteromedial approach.\(^{356}\) The results of our study thus show similar results to the previous cadaveric studies. The added value is the use of a validated method and correlation with arthroscopy, a larger and representative study population, and the identification of predictive factors. The results may also be relevant for other procedures, such as OATS and metal resurfacing inlay implants. However, for these procedures the complete OCD has to be exposed, instead of only the anterior border.

The results of chapters 4 and 5 give direction to preoperative planning protocols of the surgical approach for OCDs. The defect can be accessed by anterior arthroscopy if its anterior border is in the anterior half of the talus and ankle motion is not restricted. In doubtful cases, a CT scan of the ankle in full plantar flexion can be obtained. If the anterior border of the OCD is behind the anterior distal tibial rim with the ankle in full plantar flexion, access by means of an anterior approach will depend on the joint opening on forced plantar flexion or distraction. In case of a stiff and highly stable joint and a posterior OCD, another approach is preferred, e.g., posterior arthroscopy.

The development of new techniques and instruments may reduce the necessity of full surgical exposure. A waterjet technique has been shown to produce cone-shaped holes in the subchondral bone of human and animal cadaveric calcanei.\(^{103}\) The technique can possibly be applied via flexible tubings, allowing introduction of a small curved instrument into the joint space and creation of small holes in the subchondral bone at a perpendicular angle.\(^{103}\) However, the technique is still in its infancy and needs further development before it can be applied in clinical practice.

Although debridement and bone marrow stimulation is considered the surgical treatment of choice, there are concerns that the fibrocartilage repair tissue has insufficient durability in the long term.\(^{229,262}\) The primary aim of chapter 6 was to assess the long-term clinical and radiographic outcomes of arthroscopic debridement and bone marrow stimulation for talar OCDs. Fifty patients were evaluated after a mean follow-up of 12 years (range, 8 – 20 years). The outcomes suggested that the initial success rates of arthroscopic debridement and bone marrow stimulation for OCDs of the talus last over
time. This finding strengthens the recommendations of the treatment guideline presented in part I of the thesis. Other studies that published mid-term to long-term outcomes demonstrated similar results. These studies reported success rates of 72% to 86% after a mean follow-up of 5 to 10 years.\textsuperscript{30,44,77,128,346}

The secondary aim of chapter 6 was to determine prognostic factors that affect the long-term outcome. The study probably was not sufficiently powered to identify prognostic factors. Other studies that included more than 100 patients identified the defect size as an independent prognostic factor.\textsuperscript{76,77,82} These studies found a cutoff value of 15 mm for the defect diameter or 150 mm\textsuperscript{2} for the defect area. Larger defects posed a higher risk of poor clinical outcomes.\textsuperscript{76,77,82}

Different methods of bone marrow stimulation can be used, i.e., drilling, abrasion, and microfracturing. The latter is used the most at present. Chapter 7 described a potential pitfall in the microfracturing technique. The microfracture procedure may create small osseous fragments upon retrieval of the microfracture awl. These fragments may stay behind in the joint and act as loose bodies. Although the described pitfall could possibly influence patient outcome, this was not actually proven in the descriptive paper. Future studies, which specifically address the presence of bony particles with postoperative imaging after the microfracture procedure as well as the correlation with clinical outcome, may elucidate to what extent the particles are present and influence the clinical outcome.

Other issues related to the microfracturing technique that may require further optimization are the distance and depth of the microfracture holes. Most surgeons use intervals of 3 – 4 mm and penetrate the bone to such a depth that it leads to sufficient blood or fat droplets.\textsuperscript{223} However, no data are available on which technique leads to the best outcome.\textsuperscript{223} Further studies that compare different techniques will provide the evidence to answer these questions.

To accelerate the postoperative rehabilitation of OCDs, the advantageous effect of PEMF was postulated in chapter 2. The postoperative application of PEMF limited osteochondral graft resorption and cyst formation in sheep.\textsuperscript{47} In vitro and in vivo studies showed that PEMF stimulation leads to an increase of transforming growth factor \( \beta \), thereby improving bone development, reducing cartilage damage and increasing chondrocyte proliferation.\textsuperscript{5,47,83,98} Clinical studies showed promising results for fracture nonunion and for recovery after arthroscopic treatment of focal cartilage knee lesions.\textsuperscript{161,462} Therefore, PEMF stimulation may be effective for talar OCDs after arthroscopic treatment by producing effects that suppress inflammation, promote tissue healing, and relieve pain.\textsuperscript{436}

Chapter 8 described the detailed study protocol of a prospective, double-blind, randomized, placebo-controlled multicenter trial. It was hypothesized that PEMF-treatment after arthroscopy leads to earlier resumption of sports and an increase in the number of patients to resume sports. Sixty-eight patients were randomized to either active PEMF-treatment or sham-treatment. The final follow-up of the last patient is expected in January 2014. The outcomes of the trial will be presented in future publications. A recent review of the literature identified numerous publications supporting the hypothesis.\textsuperscript{132} The review concluded that the use of PEMF represents an innovative therapeutic approach, because this physical stimulus increases the anabolic activity of chondrocytes and cartilage explants with consequent increase of matrix synthesis. At the same time, PEMFs limit the catabolic effects of inflammatory cytokines.\textsuperscript{132}
Part III – Secondary surgical treatment with a metal resurfacing inlay implant

If the primary arthroscopic treatment of a talar OCD fails, there are various alternative treatment methods. As described in part I, current secondary methods can be successful but have several disadvantages, one being donor-site morbidity. A metal resurfacing inlay implant was developed for the treatment of secondary, localized OCDs of the medial talar dome. It has a standard diameter of 15 mm and a variety of 15 incremental offset sizes. A preliminary assessment ascertained the safety, biocompatibility, and functionality of a similar metal implant in the goat knee. Chapter 9 described a cadaveric study to test the following hypotheses: (1) a matching offset size is available for each talus, (2) the prosthetic device can be reproducibly implanted slightly recessed in relation to the talar cartilage level, and (3) with this implantation level, excessive contact pressures on the opposing tibial cartilage are avoided. The results suggested that the implant can be applied clinically in a safe way, with appropriate offset sizes for various talar domes, and without excessive pressure on the opposing cartilage.

A similar study was published 1 day after the study of chapter 9. This study investigated the effect of implantation accuracy on ankle contact mechanics. Different implantation levels (-0.5 to 0.5 mm) were tested in seven ankle specimens. Contact stresses in the talocrural joint were measured with the specimen axially loaded to 300 N. The effects of rotation and angulation of the implant were tested in a finite element analysis. This study concluded that focal resurfacing with a metal implant has the potential to restore joint mechanics in ankles with a large OCD. A recessed to flush implantation height most closely restored the original contact stress distribution. Thus, in that study, flush implantation was also found adequate, perhaps because the specimens were loaded for a shorter duration and with lower compression forces than in chapter 9. The question is whether the load-bearing capacity of the focal resurfacing implant is required. A previous study tested the consequence of increasing talar defect area on contact characteristics of the talocrural joint. This study demonstrated significant changes for lesions larger than 15 mm (i.e., decreased total contact area and increased mean pressure), but not for smaller lesions. Because the metal implant is 15 mm in diameter, recessed implantation may not be harmful to the remainder of the ankle joint, even if it is placed so deep that is does not carry any load. A recessed implant reduces the chance of overloading and damaging the opposing cartilage surface.

After the preliminary cadaveric study, the study described in chapter 10 evaluated the clinical effectiveness of the implant after failed prior surgical treatment. Twenty consecutive patients were prospectively studied. Based on a statistically significant improvement in most outcome measures, it was concluded that the metal implantation technique is a promising treatment for OCDs of the medial talar dome after failed previous treatment. These results were equalled by others. Ebskov presented similar outcomes at the 2013 annual meeting of the Danish foot and ankle society. The limitations of both studies were the relatively small series, lack of long-term follow-up, and absence of a control group. A limitation of the implant itself is the fixed diameter. In defects smaller than the implant, some healthy cartilage is sacrificed for implantation. In contrast, if the OCD is larger than the implant, some parts of the defect cannot be covered. The future development of different sizes may overcome this limitation. Furthermore, the implant was designed specifically for the medial talar dome. An implant for the lateral dome is focus of future research.
At the moment, the results of the metal resurfacing inlay implant compare with those of other resurfacing techniques such as OATS and allograft transplantation. Hangody et al. published the largest series of OATS in the talus. The authors reported that 93% of 98 patients had good to excellent clinical results on the basis of evaluation with the Hannover score, but the duration of follow-up was not reported. The main disadvantage of OATS is the donor-site morbidity, which has been reported to occur in up to 50% of cases. Allograft transplantation has gained increased attention as an alternative for large OCDs in the United States. El-Rashidy et al. and Haene et al. reported satisfactory outcomes after a mean follow-up of 3 to 4 years. However, based on the available evidence, allografts are not recommended for focal defects because of the loss of viability and stability in approximately one-third of the grafts. A disadvantage of treatments such as the metal implantation, OATS, and allograft techniques is the necessity to perform a medial malleolar osteotomy for adequate exposure and perpendicular access to the medial talar dome. An inappropriate osteotomy technique may result in a damaged weight-bearing tibial plafond, insufficient access, or in malreduction, which may negatively affect the clinical outcome. The studies in chapters 11 and 12 aimed to optimize the osteotomy technique. To obtain a congruent joint surface after refixation, the oblique osteotomy should be directed perpendicularly to the articular surface of the tibia at the intersection between the tibial plafond and medial malleolus. The purpose of chapter 11 was to determine this direction in relation to the longitudinal tibial axis for use during surgery. Forty-six radiographs and CT scans were measured. A medial malleolar osteotomy was found to be perpendicular to the tibial articular surface when directed at a mean 30° relative to the tibial axis in the frontal plane. This direction likely results in maximum congruity of the joint surface after reduction of the osteotomy. The intraobserver and interobserver reliability of the measurements were good to excellent. Hence, the methods used in this study allow for the preoperative planning of the individual patient, for example in case of abnormal anatomy. The osteotomy angle is rarely reported in the literature. Some surgeons suggested an angle of 45° relative to the tibial plafond. This is more horizontal than the direction found in our study. The 30° angle we found was subsequently used by others as a reference standard in the evaluation of their technique. Since it is difficult to visualize the intersection between the tibial plafond and medial malleolus (especially posterior) during surgery, chapter 12 described the use of a right-angled aiming probe, which is normally used for arthroscopic surgery, to identify both the posterior and anterior parts of the intersection, in order to perform a precise osteotomy. Others have used fluoroscopy to help identify the intersection, but this involves radiation and is more time-consuming. The angle and the probe, described in chapters 11 and 12, were applied during surgery and have subjectively improved the technique. However, clinical studies are required to determine if the techniques improve patient outcome. A next step in the refinement of the medial malleolar osteotomy could be the development of an intraoperative aiming device in which the use of probes and the angle are incorporated.

Part IV – Alternative treatment

Animal studies play an important role in the development of new treatments prior to introduction in clinical practice. Numerous experimental studies focused on cartilage
defects of the knee, but an experimental animal model of OCDs in the ankle joint was not available. We therefore developed such a model for talar OCDs in goats. The aim of chapter 13 was to test the developed animal model in vivo with use of autologous cancellous bone and donor DBM. It was possible to create a standardized 6-mm defect in each talus through a posterolateral surgical approach. After 12 weeks of healing, the analyses showed that most bony tissue was generated in the defects filled with autologous bone and least in the control defects. Our findings showed that a standard OCD can be created in the talus by a relatively simple procedure in a large animal that allows qualitative and quantitative evaluation. Various 2- and 3-dimensional parameters could be quantified in different regions with the combination of histomorphometry and µCT. No conclusions could be drawn on the effectiveness of the investigated materials because of the small number of goats.

Only few studies described the surgical exposure of an animal’s ankle joint. All studies used a posteromedial approach to the ankle of dogs, exposing 36% to 59% of the talar trochlea. With this approach, a medial malleolar osteotomy was sometimes required to gain sufficient exposure. Beale and Goring additionally described an anteromedial approach, exposing 43% to 64% of the medial talar trochlear ridge. Prior to the study presented in chapter 13, four surgical approaches (anteromedial, anterolateral, posteromedial, and posterolateral) were evaluated on goat cadaver ankles. The posterolateral approach was found to be the most appropriate because of the excellent exposure of the talus dome and protection of neurovascular structures.

In published studies, various artificial defect sizes have been applied. A critical size defect does not heal without treatment. In the presented ankle model, the defects were sized 6 mm in diameter and depth. A goat study investigating the natural course of knee defects showed that 6-mm defects do not heal spontaneously within 1 year but rather develop into cystic lesions. In the present model the control defects did not heal either, confirming that the created defect in the talus was appropriate.

Some points for improvement of the model were encountered. There was variation in outcome between the animals. The radiographs were useless for analysis of repair because the OCDs were not consistently visible. The fluorochrome labels were not always detectable in the histologic sections. The duration of follow-up was possibly too short for full remodeling of the defects, as evidenced by areas with osteoid and osteoblasts. It was concluded that the model, with a few adjustments such as a paired analysis and longer follow-up, can be used in future experiments investigating alternative treatment methods for talar OCDs.

DBM and platelet-rich plasma (PRP) possess the possibility of a one-step, minimally invasive procedure that stimulates biologic repair. Previous studies showed the effectiveness of DBM, e.g., in ankle fusion, tibial defects, and OCDs of rabbit knees. Platelet-rich plasma (PRP) contains growth factors that could possibly enhance the treatment effect of DBM. The purpose of chapter 14 was to evaluate the effectiveness of DBM with and without PRP in the treatment of 32 OCDs with use of the previously developed caprine model. In contrast to our hypotheses, none of the analyses revealed statistically significant differences between the groups after 24 weeks.

The absence of a positive effect may be caused by various factors. The effectiveness of DBM is dependent on donor age, processing technique, and sterilization procedure. The DBM used in chapter 14, however, has proven osteoinductive and osteoconductive properties. Although the use of DBM has resulted in advantageous outcomes for
nonunions and segmental defects of cysts of long bones,\textsuperscript{107,117,145,171,392} the literature for intra-articular pathology is scarce.\textsuperscript{94,140} Perhaps the joint environment precludes the proper healing response of DBM by the ingress of fluid into the repaired area.\textsuperscript{433}

PRP is a promising (adjuvant) treatment for OCDs.\textsuperscript{226,362} Multiple in vitro and in vivo studies delineate the potential of PRP to improve OCD repair.\textsuperscript{362} The in vitro literature indicates that this biological adjunct may increase chondrocyte proliferation as well as synthetic capability, while limiting the catabolic effects of an inflammatory joint environment.\textsuperscript{10,233,287,418} In a rabbit model, the addition of PRP showed improved healing of OCDs treated with microfracture surgery.\textsuperscript{284} Human studies have reported variable effects of PRP injections alone as well as in addition to surgery. Not all studies concluded that PRP had a positive effect on cartilage repair.\textsuperscript{226,363} The vast majority of studies investigated the knee. Extrapolation to the ankle joint is unreliable because of the differences in cartilage properties, joint congruence, and response to injury.\textsuperscript{26,181,234,311} One study specifically investigated PRP for talar OCDs.\textsuperscript{280} Thirty patients received three weekly intra-articular injections of hyaluronic acid or PRP. After 28 weeks of follow-up, the outcomes were significantly better for the PRP group in controlling pain and re-establishing function.\textsuperscript{280} However, the aspect of the repair tissue was not investigated. The specimens in our animal study showed no improvement in healing of the tissue. Perhaps the combination of PRP and DBM is suboptimal, as their interaction is not yet well understood.\textsuperscript{324} Furthermore, the concentration of PRP varied among the goats, but no significant differences in outcomes were found between high and low concentrations. Further studies are indicated to determine the ideal preparation of DBM and the optimal concentration of PRP as well as their interaction before they can be uniformly investigated.

Part V – Outcome measures

Outcome assessment is critical in evaluating the efficacy of orthopaedic procedures. Many outcome scores have been used to assess the effect of interventions for OCDs. Chapter 15 discussed frequently used clinical outcome scores and postoperative imaging studies. Some clear recommendations for the use of outcome scores were provided. However, it was stressed that none of the clinical outcome scores has been investigated psychometrically in the specific patient population with a talar OCD. There is a need for reliable and valid outcome measures that have been investigated in the target population and are available in different languages.

The Foot and Ankle Outcome Score (FAOS), as used in chapter 10, is one of the few validated outcome measures for ankle pathology. The score was available in Dutch and other languages but not in German. For the purpose of conducting clinical studies in Germany, a translation and validation study of the German FAOS was performed. This study was presented in chapter 16. After forward and backward translation, the final translation of the FAOS was validated in a series of 150 German patients with chronic foot and ankle-related problems. The findings indicated that the translated German version of the FAOS is a reliable and valid instrument for use in foot and ankle patients. Although the German version of the FAOS was not used in the clinical study investigating the metal implant (chapter 10), the results of chapter 16 enables its use in future international multicenter studies and allows for the comparison of studies from different countries. Translating and validating the FAOS into more languages as well as determining the minimal clinically important change will further expand its applicability.
Conclusions and future directions

The treatment of talar OCDs provides a challenge for the orthopaedic surgeon. In the recent past, there was discussion in the orthopaedic community on the optimal treatment plan. Although bone marrow stimulation had been applied for a long time and was considered the primary treatment, surgeons questioned the durability of the fibrocartilaginous repair tissue. Furthermore, it was sometimes unclear which surgical approach to the OCD was most appropriate. Previous secondary treatments had disadvantages such as morbidity of the donor site and limited availability. To investigate alternatives, only knee animal models were available. Lastly, a great diversity of outcome measures was available to report clinical results of talar OCD treatment. The choice for the outcome measure used seemed arbitrary.

This thesis has contributed to the treatment of patients with talar OCDs in various ways. The literature was reviewed and a treatment algorithm was proposed. The long-term outcomes of arthroscopic bone marrow stimulation reassured the durability of the technique and set the reference standard for other procedures to equal. Evidence-based directions for preoperative planning by CT scanning were provided. CT scans showed that almost half of the talar dome is accessible in the anterior working area with the ankle in full plantar flexion. The trial on acceleration of the rehabilitation with PEMF is only months before final follow-up. A novel metal implantation technique was prospectively investigated. Most patients had good clinical outcomes at a mean follow-up of 3 years. The implant can be considered a valuable alternative to current secondary treatment methods. The open surgical approach with use of the medial malleolar osteotomy was refined. When directed at a mean 30° angle relative to the long tibial axis, the osteotomy enters the joint perpendicularly to the tibial cartilage at the intersection with the medial malleolus. A goat model was developed for the ankle joint, which allows reproducible creation of a talar OCD and qualitative and quantitative analysis. DBM and PRP were investigated with use of the developed goat model. They were not effective in the treatment of goat OCDs compared to control defects. Finally, various outcome measures were reviewed, and a guideline was provided. The German version of the FAOS was translated and validated.

Several recommendations can be made for treatment of talar OCDs on the basis of the thesis and the current literature. Based on the long-term outcomes, arthroscopic bone marrow stimulation remains the primary surgical treatment for chronic OCDs up to 15 mm. If the primary treatment fails, various secondary treatment options remain, including OATS, (matrix-induced) ACI, cancellous bone grafting, and metal resurfacing. The choice depends on patient and lesion characteristics as well as surgeon preferences. Any malalignment of the hindfoot should probably be corrected concomitantly. Salvage procedures for refractory defects are allograft transplantation, ankle arthrodesis and total arthroplasty.

Despite the advancements achieved by the studies reported in this thesis, there is an ongoing debate among orthopaedic surgeons. There are still many possibilities for future research to further ameliorate the perspective of patients with a talar OCD. Arthroscopic bone marrow stimulation has been proven to be effective over the years. Future research may further increase the success rate of the technique. The outcomes of bone marrow stimulation may be improved by identifying the most effective depth and distance of subchondral bone penetration. Additionally, in cases where the OCD is difficult to reach, the development of new techniques and instruments may assist the surgeon in
treating the OCD adequately with minimal soft-tissue damage. The use of pressurized water jets is a promising development in this area.\textsuperscript{103} The presence of postoperative bony particles after the microfracture procedure should be identified with postoperative imaging techniques to determine to what extent the particles are present and whether clinical outcome is affected. The metal resurfacing inlay implant was found to be a promising option for the treatment of secondary OCDs of the medial talar dome. However, more patients, longer follow-up, and a control group will better determine the place of the implant in the treatment of talar OCDs. The development of additional implant sizes as well as an implant for the lateral talar dome will expand its use. Correction osteotomy for OCDs in malaligned ankles seems a promising solution but clinical studies are required. Cell-based (adjunct) therapies may become more attractive in the future.\textsuperscript{362} PRP was not beneficial in the study described in chapter 14, but its use was promising in other studies.\textsuperscript{226,363} Determining the optimal concentration and application is important before the clinical effect of PRP can be evaluated reliably. An alternative cell-based therapy is bone marrow aspirate concentrate, but clinical data are scarce.\textsuperscript{150,214,362} The ultimate goal of OCD treatment is to regenerate the complete osteochondral unit by a construct that results in repair of the subchondral bone as well as an integrated layer of hyaline cartilage. However, inferior methods will have to be used until such an ideal treatment is available.

In the current era of evidence based medicine, there is still no optimal treatment for talar OCDs. Great diversity and variability between studies provide the surgeon interesting choices with an important role for the patient and his or her demands. Sufficiently powered, randomized controlled trials with uniform methodology and validated outcome measures, as well as the optimization of current treatment methods and development of new methods, may form the foundation of the optimal treatment plan for future talar OCDs.