Fiber-reinforced fixation implant for proximal interphalangeal joint arthrodesis shows implant bio-integration at 1-year follow-up

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ABSTRACT

Background: A new bio-integrative fiber-reinforced implant (OSSIOfiber®) Hammertoe Fixation Implant, OSSIO Ltd., Caesarea, Israel) was developed for proximal interphalangeal joint (PIP) correction-arthrodesis. The main purpose of this clinical study was to assess implant bio-integration at 1-year follow-up.

Methods: Twenty-four patients, previously treated for a Hammertoe deformity using the bio-integrative, fiber-reinforced implant, were enrolled in this follow-up study. One-year follow-up included clinical examination, patient reported outcomes, radiographs, Magnetic Resonance Imaging (MRI) and bio-integration scoring.

Results: Proximal interphalangeal joint (PIP) radiographic fusion rate was 92% (n = 22). MRI was analyzed for 24 (100%) patients. In 100% of patients (n = 24), the border between implant and surrounding tissue was scored as partially visible. There were no cyst formation or fluid accumulation findings. Mild bone edema was detected in 29% (n = 7) and is attributed to the chronic distribution of forces due to chronic abnormal gait and posture. None of the edema findings were considered as adverse implant-related finding. The mean bio-integration score was 7.71 ± 0.46.

Conclusions: This study demonstrates safe bio-integration of the newly developed fiber-reinforced implant at 1-year follow-up without negative side effects.

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1. Introduction

Kirschner wire (K-wire) fixation is considered the standard method for proximal interphalangeal joint (PIP) correction-arthrodesis for correction of hammertoe deformity [1–4]. K-wire fixation has several limitations, such as lack of rotational stability (as usually only one wire is used), K-wire site infection, wire migration, breakage, non-union, malunion and necessity for K-wire removal [1,2,4–6]. A variety of intramedullary internal fixation devices, which do not require removal, have been developed to overcome these limitations and improve PIP correction-arthrodesis outcomes. These devices are made of a variety of resorbable and permanent materials [1,3,7–21]. Specifically, implant resorption is considered a beneficial factor as it eliminates the need for hardware removal procedures [19,8–21]. However, the resorption process can be associated with an inflammatory response [4,19,8–21]. For this reason, integration or better bio-integration with the surrounding tissue, without adverse inflammatory reaction, is an important goal for the ongoing development and wider acceptance of non-permanent orthopedic devices. A bio-integrative material composed of continuous reinforcing mineral fibers, bound together by a degradable polymer [poly (l-lactide-co- dl-lactide), PLDLA] matrix was used to develop a PIP fixation implant (OSSIOfiber® Hammertoe Fixation Implant, OSSIO Ltd., Caesarea, Israel, Fig. 1a and b) [4,22,23]. This novel implant demonstrated favorable PIP fusion rates without complications in a previous prospective, multicenter, clinical trial [4]. This first-in-human study was focused on joint fusion and safety with longest follow-up of 26 weeks [4], and bio-integration effect was not primarily assessed. The main purpose of this follow-up study was to analyze the bio-integration process at 1-year follow-up with inclusion of Magnetic Resonance Imaging (MRI) and a newly introduced bio-integration score.

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follow-up study. Further inclusion and exclusion criteria are shown in Table 1. Recruitment was set at a minimum of 75% from original study cohort of 25 patients. This study adhered to the Declaration of Helsinki and was approved by the local ethics committee at each institution.

During the screening visit, the patient demographic data, medical history, medication information and clinical assessment of the operated foot were recorded. Foot and toe assessment as well as pain score (0–10), Foot and Ankle Ability Measure Activities of Daily Living Subscale (FAAM-ADL, 0–100) and percentage level of functioning (0–100) were performed (“Baseline”) [4,24]. Radiographs were taken and evaluated and computed tomography (CT) scans were ordered at the surgeon’s discretion [4].

2.2. Implant

The bio-integrative hammertoe fixation implant (OSSIOfiber® Hammertoe Fixation Implant, OSSIO Ltd., Caesarea, Israel) is comprised of continuous, reinforcing mineral fibers (SiO₂, Na₂O, CaO, MgO, B₂O₃, and P₂O₅, approximately 50% w/w), which have been shown both in vitro and in vivo to support bone growth and regeneration and are bound together with PDLA polymer resin (approximately 50% w/w) [23]. Controlled and gradual bio-integration into the surrounding bone without adverse inflammatory response, has been previously shown [22]. The implant used in this study has a hexagonal cross-section with a nominal dimension of 2.9 mm diameter and 19 mm length (Fig. 1a). The ribbed design allows for implant fixation in the phalangeal canal of the toe. The internal structure of the implant consists of layers of oriented continuous fibers (Fig. 1b) that should provide mechanical strength through the bone healing process.

2.3. Surgical procedures [4]

Two foot and ankle surgeons performed all surgeries at three different sites. Each surgery took place within 30 days of enrollment or pre-screening radiographs (Fig. 2a and b). On the day of the surgery, patient eligibility was confirmed, medications information was recorded, and a foot and toe assessment was performed. For the surgery, local and/or regional anesthesia was administered. Following the site standard of care, some patients received prophylactic antibiotic. During the surgery, fluoroscopy imaging was used. A straight longitudinal midline approach over the PIPJ was used. Resection of both joint surfaces followed. The proximal phalanx diaphyseal canal and the middle phalanx diaphyseal canal were drilled with 2.9 mm diameter to the appropriate depth (Fig. 3a). Using the implant holder, the proximal end of the fiber-reinforced hammertoe fixation implant was introduced into the proximal phalanx, parallel to the long axis of the drill hole to prevent bending (Fig. 3b). The middle phalanx was manually reduced over the distal end of the implant while applying slow, steady pressure until bone-to-bone contact was reached (Fig. 3c). After confirming that the implant was properly fitted and...
fixated to the bone, the surgeon completed the procedure using routine soft tissue closure.

2.4. Aftertreatment [4]

Dorsoplantar, lateral and lateral oblique radiographs were taken immediately following the procedure. All patients were fitted with a protective shoe for six weeks. Patients were advised to elevate the foot for the early postoperative days. At one week postoperatively patients returned to clinic for a dressing change and wound evaluation.

2.5. Follow-up

Post-operative follow-up to 26 weeks was performed and analyzed in the previous study of same cohort [4]. The one-year follow-up included clinical examination, radiographs, pain score, FAAM-ADL and MRI assessment (minimum resolution 1.2 mm, Table 2). A MRI based bio-integration score was developed for this study (Table 3). MRI images were reviewed and analyzed by a certified, independent reviewer; each assessment was performed twice for intra-observer reliability.

2.6. Statistics

Excel Version 1809 (Microsoft, Redmont, WA, USA) was used for the statistical evaluation of intra-observer reliability of MRI assessment (paired t-test, heteroscedatic).

3. Results

3.1. Patients

From a potential cohort of 25 patients, 24 were screened and enrolled in this follow-up study, including 23 female (96%) and 1 male (4%). The mean age of the cohort was 64.9 ± 7.3 (range, 50–75) years. Mean preoperative scores were as follows: pain 5.3 ± 2.5, FAAM-ADL 73.8 ± 19.4 and percentage level of functioning 69.4 ± 16.9.

3.2. Procedures

The hammertoe deformity affected the second toe in 23 patients (96%), and the third toe in one patient (4%). Nineteen patients (76%) underwent concomitant procedures for first ray deformities, including corrective osteotomies and first MTP joint fusion. Fig. 2a–g shows radiographs and MRI of one representative case.

3.3. Follow-up

All 24 patients (100%) completed the 1-year follow-up. Pain scores improved to 0.3 ± 1.08, FAAM-ADL to 96.3 ± 6.6 and percentage level of functioning to 96.0 ± 5.9. 100% of subjects were either very satisfied (19/24) or satisfied (5/24) with the procedure outcomes. Radiographs confirmed fusion in 92% (n = 22) PIPJ at 1-year follow-up. Table 4 shows the results of the MRI assessment for the 24 patients (100%). The implant was visible in all patients. In 100% of patients (n = 24), the border between implant and surrounding tissue was scored partially visible. There were no cyst formation or fluid accumulation findings. Mild bone edema was detected in 29% (n = 7). None of the edema findings were considered as implant related. The mean bio-integration score was 7.71 ± 0.46 (Table 3). The intraobserver reliability (test–re-test) was sufficient (each p > 0.16).
Fig. 3. a–d. Intraoperative situs. A 2.9 mm diameter, marked drill to create tunnel in the proximal phalanx (a). Implant insertion with inserter retrograde into proximal phalanx (b). Implant distal side visible following insertion into the proximal phalanx (c). After mounting the middle phalanx onto implant gradual pressure is applied until bone to bone contact is achieved (d).

Table 2
MRI protocol.

| Series I  | TR 3400 /TE 4000 msec; BW 31 kHz; ETL 7–9; NEX 2; FOV 10 cm; SL 3–3.5 mm; matrix 512 × 320 |
|-----------|-------------------------------------------------------------------------------------------------|
| Series II | Sagittal Oblique FSE angled to the operated toe metatarsal shaft |
| Series III| Sagittal Oblique FSE 2nd through 5th MT shafts |
| Series IV | TR 4000/TE 34 msec; BW 31.2 kHz; ETL 7–10; NEX 2; FOV 15 cm; SL 2.5–2.8 mm; matrix 256 × 192 |
| Series V | TR 4000/TE 34 msec; BW 31.2 kHz; ETL 7–10; NEX 2; FOV 15 cm; SL 2.5–2.8 mm; matrix 256 × 192 |
| Series VI | Sagittal STIR |

4. Discussion

This is the first study analyzing bio-integration of an implant for osteosynthesis. Many implants are classified as “resorbable”, “absorbable” or “degradable” [25–29]. Even Magnesium-alloys and Polyvinyl implants are considered as degradable which is theoretical, yet extremely unlikely, as these materials are unable to degrade during a human’s lifetime [27,30]. When considering an orthopaedic fixation device, surgeons are looking for safe and effective methods. The ideal implant should integrate with the surrounding tissue without any negative side effects. In this study, we could prove bio-integration of the newly developed implant at 1-year follow-up without negative side effects. This observation is the main finding of the study and suggests that further, and up-to-complete bio-integration will occur at a later stage.
Table 3
Bio-integration score.

| Parameter                              | Points |
|----------------------------------------|--------|
| Border between implant and bone        |        |
| Not visible                            | 4      |
| Partially visible                      | 2      |
| Clearly visible                        | 0      |
| Bone edema                             |        |
| None                                   | 2      |
| Mild                                   | 1      |
| Moderate/massive                       | 0      |
| Cyst formation                         |        |
| No                                     | 2      |
| Yes                                    | 0      |
| Fluid accumulation                     |        |
| No                                     | 2      |
| Yes                                    | 0      |
| In total                               |        |
| Minimum 0 = no bio-integration, maximum 10 = complete bio-integration. |

Table 4
Bio-integration Score Results.

| Parameter                              | Points (mean ± std) |
|----------------------------------------|---------------------|
| Border between implant and bone (0–4)  | 2.0 ± 0             |
| Bone edema                             | 1.71 ± 0.46         |
| Cyst formation                         | 2 ± 0               |
| Fluid accumulation                     | 2.0 ± 0             |
| Total score (0–10)                     | 7.71 ± 0.46         |

std, standard deviation.

4.1. Assessment of bio-integration

Different options for the assessment of bio-integration were discussed including CT and MRI. CT has a clear advantage of a much higher resolution (down to 0.1 mm), whereas the typical resolution of MRI is 3 mm which would not allow for an adequate assessment of an implant with a nominal dimension of 2.9 mm (Fig. 2a) [31]. The whole implant could theoretically be missed between two slices, as all other relevant structures and findings including cyst formation, bone edema, and fluid; the potential advantage of MRI in relation to CT is the better detection of these relevant findings. Based on a special scanning protocol, we could achieve a resolution/slice thickness of 1.2 mm which we considered as adequate and lessens the potential risk of missing important data (Fig. 2g).

4.2. Development of a degradation score

We were not aware of a scoring system for implant degradation or bio-integration; therefore, we created a system for this study (Table 3). We considered optimal bio-integration as a non-visible border between implant and bone, and lack of fluid, implant-related bone edema or cyst formation. This finding results in a maximum bio-integration score of 10 points. In contrast, clearly visible border between bone and implant, with evidence of cyst formation, implant-related bone edema and fluid result in a minimum bio-integration score of 0 points. The average bio-integration score in our study was 7.71 ± 0.46. We consider this a very favorable result even though we cannot compare this with the literature based on missing comparable data. However, the implant was still visible at one year in all cases which was an expected finding, as full degradation was not expected at the 1-year timepoint. The intra-observer reliability of the bio-integration score was sufficient to consider this score a reproducible measure. Mild bone edema was detected in 7 of 24 subjects – this finding is very common in older patients and in post-orthopaedic procedures of the foot; it is often attributed to the chronic distribution of forces due to abnormal gait and posture or foot malalignment [32]. None of the edema findings were considered as adverse implant related event.

4.3. Shortcomings of the study

Shortcomings of this study are low case number, missing control group, and the relatively short follow-up time. The case number was calculated with a focus on safety and implant performance. A missing control group is a methodological shortcoming as in many other studies that we cannot invalidate. A follow-up time of 1 year does not meet some international scientific standards for clinical studies with a minimum of 2 years. However, this follow-up study did not primarily focus on clinical outcome but on bio-integration. The results demonstrate that substantial bio-integration has occurred at one year, even though not complete. Another potential limitation is the assessment method of bio-integration as discussed above. The use of a non-validated degradation score is also a potential shortcoming, but a validated score does not yet exist.

In conclusion, this is the first study analyzing bio-integration of an implant for osteosynthesis. We could prove the bio-integration of the newly developed fiber-reinforced implant at 1-year follow-up without negative side effects. The implants were partially bio-integrated at the 1-year timepoint. An ongoing study project is desired to follow these patients at best until complete bio-integration is reached.

Conflict of interest

Luke D. Cichinelli, Martinus Richter and Stuart Miller are consultants of Ossio. Martinus Richter is consultant of Curvebeam, Geistlich, Intercus, and Implants International, proprietor of R-Innovation, and shareholder of Curvebeam. The study was funded in part by Ossio Ltd., Caesarea, Israel.

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