Intramedullary nailing of forearm shaft fractures by biodegradable compared with titanium nails: Results of a prospective randomized trial in children with at least two years of follow-up

Linda Korhonen, Marja Perhomaa, Antti Kyrö, Tytti Pokka, Willy Serlo, Juhani Merikanto, Jaakko Sinikumpu

PII: S0142-9612(18)30642-2
DOI: 10.1016/j.biomaterials.2018.09.011
Reference: JBMT 18882

To appear in: Biomaterials

Received Date: 19 April 2018
Revised Date: 2 September 2018
Accepted Date: 7 September 2018

Please cite this article as: Korhonen L, Perhomaa M, Kyrö A, Pokka T, Serlo W, Merikanto J, Sinikumpu J, Intramedullary nailing of forearm shaft fractures by biodegradable compared with titanium nails: Results of a prospective randomized trial in children with at least two years of follow-up, Biomaterials (2018), doi: 10.1016/j.biomaterials.2018.09.011.

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Intramedullary Nailing of Forearm Shaft Fractures by Biodegradable compared with Titanium Nails: Results of a Prospective Randomized Trial in Children with at Least Two Years of Follow-up
ABSTRACT

There are disadvantages in Elastic Stable Intramedullary Nailing (ESIN) of forearm-shaft fractures, such as the need of implant removal. Biodegradable Intramedullary Nailing (BIN) is a new technique developed for these fractures. We hypothesized that there is no difference in rotational ROM between the patients treated by BIN vs. ESIN. A randomized, controlled clinical trial included patients, aged 5–15 years, requiring surgery for forearm-shaft fractures. Biodegradable polylactide-co-glycolide (PLGA) nails (Activa IM-Nail™, Bioretec Ltd., Finland) were used in 19 and titanium nails (TEN®, SynthesDePuy Ltd., USA) in 16 patients. Rotational ROM of forearm after two years was the primary outcome. Elbow and wrist ROM, pain and radiographic bone healing were secondary outcomes.

Forearm rotation was mean 162° and 151° in BIN and ESIN groups, respectively (P=0.201). No difference between the groups was found in any other ROMs. Three cases in the ESIN vs. none in the BIN group reported pain (P=0.113).

There was no clinically significant residual angulation in radiographs. Two adolescents in the BIN group vs. none in the ESIN (P=0.245) were excluded because of implant failure; another two with complete bone union suffered from re-injury. Therefore, satisfactory implant stability among older children needs to be studied.

Level of evidence: I
INTRODUCTION

The incidence of forearm shaft fractures has increased in recent decades and they represent about 10–15% of all fractures in children. Most forearm fractures in children can be treated nonoperatively, resulting in excellent long-term outcomes. However, comminuted, unstable, open fractures and fractures with major soft tissue complications justify surgical treatment. At present, elastic stable intramedullary nailing (ESIN) is the gold-standard method of surgical treatment of forearm shaft fractures. Compared with open reduction and plate fixation, ESIN is less traumatic and results in better cosmesis. It shows an equally good union rate and is also feasible when open reduction is needed.

Although being rare when appropriate technique is used, some weaknesses have been reported in ESIN. A metallic implant predisposes the patient to bacterial infections, may cause local pain and soft-tissue irritation and may interfere with radiological imaging. Radial nerve lesion, delayed union, nonunion, re-fracture and compartment syndrome may occur. The long-term effects of these implants are not yet known. Therefore, the implants are traditionally removed 3–6 months postoperatively. Removal predisposes children to operation-related risks and causes psychosocial stress. The cost of implant removal is approximately $1,900 in a developed country. There are also some institutions that prefer leaving the implants or removing only symptomatic ones even though, it is not widely understood how metallic implants affect the natural modeling of the forearm. Particularly the changes in lateral bowing of the radius during growth, may affect rotational movements in long-term. These problems are not faced if the implants are removed in early phase.

There has been increasing interest in biodegradable materials in trauma surgery. A new minimvasive procedure to treat unstable forearm fractures with Biodegradable Intramedullary Nailing (BIN) has been developed. Biodegradable nails are designed to maintain mechanical strength but to be absorbed during bone healing. An investigational implant is an ultra-high-strength biodegradable intramedullary nail of poly(lactide-co-glycolide) (PLGA) with a tricalcium-phosphate (β-TCP) marker, designed and manufactured for the purpose by Bioretec Ltd. (Hermiankatu 22, Tampere, Finland). It was mechanically based on the corresponding (short) pins that have been used in many indications in traumatology. Preclinical testing was not needed; PLGA has previously been shown to be safe and biocompatible in preclinical work in animals and in human medical use. The implant was planned to be feasible in both radial- and ulnar-shaft
fracture repair. The outcome of use was to be comparable with that of metallic intramedullary nails; restoration of the functional range of motion of the elbow and forearm. The highly elastic nails allow free physiological remodeling of the forearm bones after fracture healing, thereby contributing to the function of the nonsynovial forearm joint. Nails of three diameters (2.0, 2.7 and 3.2 mm) have been produced and they are all 400 mm in length. Owing to a hydrolytically activated memory effect, the diameter of the implant increases and its length decreases by 1%–2% after being introduced into human tissue. This is assumed to increase the stability of fixation. Because the biodegradable implant is highly elastic and completely follows the natural form of the bone it can’t hold a curved form similar to pre-bended titanium nail. External support by casting may be important to hold alignment. The BIN itself is straight and the tip of the nail is not curved (FIGURE 1). Degradation of the implant material occurs both by hydrolysis and by way of physiological pathways. The operative procedure is mostly similar to that in ESIN stabilization. However, reaming through the whole medullary cavity until the planned end of the rodding is recommended, after which the implants are introduced by pushing and slightly tapping the nails into the cavity. A special lockable hammer instrument is used (FIGURE 1). Regardless of the implant material, the forearm may be immobilized for 4–6 weeks, depending both on stability achieved and on institutional practice. In this study, all patients were immobilized for the coherence of the study population.

The aim of this study was to assess the BIN technique in treating unstable childhood radius and/or ulna shaft fractures, compared with titanium elastic stable intramedullary nailing (ESIN) and thus, test the hypothesis that there is no difference in two-year rotation range of motion between the patients treated by BIN vs. ESIN.
MATERIALS AND METHODS

Study design and patients

This prospective, randomized, clinical trial (RCT) was a two-center study, performed in Oulu University Hospital, Oulu, Finland, and the Central Hospital of Päijät-Häme, Lahti, Finland in 2011–2017. Patients were enrolled between November 2011 and January 2015; the enrolment time was 3 year and 3 months. The last follow-up visit was executed in January 2017. Patients, aged between 5 and 15 years, who suffered from single- or both-bone forearm shaft fractures requiring surgical fixation were invited. The eligible participants were randomized into two groups (by using sealed envelopes) to be treated by BIN or ESIN. Patients with open fractures, significant soft-tissue injury, pathological fractures or previous fracture or infection in the forearm were excluded. In addition, patients with metabolic bone diseases, systemic disease or medication affecting bone quality or resistance to infection, or fractures older than seven days were predominantly excluded. All information was collected via standardized questionnaires. The patients were investigated four weeks, three months, six months and two years postoperatively and contacted by phone one year postoperatively. The radiographs were taken in every follow-up visit and analyzed by an experienced pediatric radiologist, familiar with childhood trauma. Metallic nails were removed six months postoperatively.

It has previously been reported that pronation-supination ROM after ESIN is 153° (mean) while the normal ROM in that age-group is 170°. The latter was assumed to demonstrate ROM in the BIN patients, as BIN was thought to be elastic enough to contribute to normal remodeling of the forearm after fracture healing. We calculated that 13 patients per group was needed, by using 17° as clinically important difference and 15° standard deviation (SD) and with alfa level of 0.05 and power of 80%. To compensate the possible drop-outs during the 2-years follow-up, we decided in advance to continue recruitment beyond the satisfactory sample of 26 patients by exceeding the enrolment by minimum 20% in both groups. Therefore, the recruitment was interrupted at the time it became certain that 20% exceeding of the groups was reached; however, at the time of interruption the other one of the two groups had increased up to N=19. The final exceeding was thus 35% (N=35/26). (FIGURE 2).
The mean age of the patients was 10.1 years (range 5–15, SD 2.5 y). Their mean height was 143.6 cm (range 116–173 cm, SD 16.0 cm) and weight 36.3 kg (range 20–67 kg, SD 11.8 kg). The patients in the two groups were the same age (P=0.569).

33 (94%) patients suffered from diaphyseal both-bone fracture and 2 had isolated diaphyseal radius fracture. Most of the fractures belonged in AO type 22r-D/4.1, 22u-D/5.1 (40%) or 22-D/5.1 (29%) and the rest were either 22-D/4.1 or 22r-D/5.1, 22u-D/4.1. The two single bone fractures were AO type 22r-D/4.1. Seven patients (20.0%) were treated by stabilizing the radius only; four of them were in the BIN group and three in the ESIN group (P>0.999).

**Primary outcome variable**

The primary outcome in the study was the rotational range of motion arch (ROM) at the two-year mark.

**Secondary outcome variables**

The other outcomes were ROM of the elbow and wrist, general pain, and pain at the fracture site two years after the injury. The motion ranges are reported as mean values, and we used the classification of Price (Table 1). Pain was expressed on a visual analogue scale (VAS, 0–100 mm) in mm ± SD. Plain radiographs of the forearm in anterior–posterior (AP) and lateral projections were obtained at follow-up visits. Fracture reduction (mm), angular deformity (degrees ± SD), radiographic fracture healing (union, delayed union, nonunion) and fracture malunion, limb-length discrepancy were analyzed. The angulation was determined drawing the lines align with the axis of both bone fragments after which the angle between the two lines was then calculated (FIGURE 3).

Radiographic examinations were carried out repeatedly to assess the bone-healing process and to note treatment-related complications (e.g. implant-related osteolysis and intramedullary nail (IM) failure). Regarding the bone healing, callus formation (in all cortexes of both bones) and fracture line visibility were analyzed in every follow-up visit. The elements of the Lane-Sandhu scoring system for fracture healing were used in evaluating radiographs. Biodegradation of the investigational device was evaluated by MRI in a randomly selected subgroup of patients (N=13).

Other outcome variables included operation time from incision to casting, length of hospitalization (days) and complaints in daily living. All surgery-related infections, intra-operative complications related to fixation hardware, osteolysis, bio-incompatibility reactions and mechanical implant
failure (loss of reduction) were registered to ensure the safety of the device. Drop-outs were analyzed in detail.

Randomization and masking

A study assistant provided by the sponsor and not involved in the treatment was responsible for randomization, using varied block sizes to achieve 19 sealed envelopes per group. The envelopes were delivered to the study centers as required. After obtaining signed informed consent, a nurse at the ward not involved in the treatment of the patient opened one envelope for the operating surgeon. Parents and children were not blinded to the treatment and the orthopedic surgeon and the radiologist examined and analyzed the patients without masking. The radiographic analyses of all imagines in both study institutions were done by the same radiologist, to avoid inter-rater error in the measurements. Intra-rater validity was evaluated by measuring lateral angulation of the radius bone twice in the radiographs. The measurements were done in the separate settings and the radiologist (MP) was blinded to the previous measurements. Intra-rater reliability was found to be excellent, the ICC was 0.941.

Statistical methods

Differences in continuous variables between the two treatments were analyzed by Student’s t-test for normal distributed variables and by Mann-Whitney U test for skewed variables. The chi-square test or Fisher’s exact test was used to compare distribution between classified variables, and the Standardized Normal Deviate (SND) test in testing differences in proportions. Intra Class Coefficient (ICC) was used to evaluate intra-rater validity of radiographic measurement. Less than 5% was considered to be the level of statistical significance (P<0.05). All tests were two-sided and 95% confidence intervals were used. Statistical analyses were performed by using SPSS version 24 software (IBM-SPSS Inc., USA) and StatsDirect Ltd. 2013 version 3.1 (Sale, Cheshire, England).

Ethical aspects

The study plan was approved by the Medical Ethics Committee and the Hospital Ethics Committee of Tampere Hospital District, Tampere, Finland (§R09231/2009) and recorded in the annals of the Northern Finland Hospital District, Oulu, Finland. The study is registered in Clinical Trials.gov
(NCT03474900) and the National Supervisory Authority for Welfare and Health (Valvira) approved the implant for use in this study. Informed consent to participate was obtained from all patients and their guardians; they had the right to interrupt participation at any time. Preclinical testing was not needed: PLGA has previously been shown to be safe and biocompatible in preclinical work in animals\textsuperscript{44,45} and in human medical use\textsuperscript{43,46}. Further, there is wide experience of its use in other indications in trauma surgery, also in children\textsuperscript{44,54}. Implant-related complications have been rare\textsuperscript{55,56}. The first potential patient was operated using the study implant to ensure the feasibility of the method and the implant in practice but was not included in the study, according to the study plan.

**FUNDING**

The implants were manufactured and provided by Bioretec Ltd., Finland. Economic support was received from Oulu University Hospital as well as from Non-Profit Foundations. Jaakko Sinikumpu has received a grant to participate in a scientific conference (European Paediatric Orthopaedic Society Annual Meeting, 2018) and to scientific working by Bioretec ltd. None for other authors. Any of the funding bodies did not play a role in investigation, data analyses or writing the manuscript. The funds were used for salaries of the researchers and other co-workers like research nurses.
RESULTS

Range of motion of the forearm, elbow and wrist, and pain

No difference was found in any ROMs between the BIN and ESIN groups, while injured sides in both groups were analyzed. In addition, the loss of ROM as compared with the uninjured side was calculated and there was no difference in the outcomes between the groups. The primary outcome, ROM of forearm rotation in the injured side, was a mean of 162° (range 105°-200°, SD 22°) in the BIN group and 151° (range 90°-180°, SD 23°) in ESIN group (P=0.201).

Elbow flexion-extension ROM was a mean of 154° (range 132°-175°, SD 11°) in BIN patients and 148° (range 130°-185°, SD 15°) in the ESIN (P=0.233) patients. Flexion-extension ROM of the wrist was 150° (range 110°-180°, SD 20°) and 150° (range 95°-110°, SD 20°) in these groups, respectively (P=0.872). None of the movements differed significantly when compared between the groups. All cases achieved excellent or good results when classified according to Price53.

At two years, some pain at the fracture site (VAS) was reported in 3/16 cases, all treated with ESIN, compared with 0/16 in the BIN group (difference 19.0%, 95% CI -4.1%–43.4%, P=0.113). Pain seemed to be greater postoperatively in the ESIN group (VAS=62.2 mm) than in the BIN group (VAS=40.9 mm) (P=0.050), and slightly greater at follow-up.

Radiographic and MRI findings

Every patient presented excellent bone union at two years (FIGURE 4); complete callus was seen in four cortexes and the fracture line was invisible (Table 2). There was no abnormal soft-tissue reaction in the fracture surroundings or osteolysis in the stabilized bone in the two-year MRI (N=13). The biodegradable implants were still visible in all, but partially (N=3) or almost completely (N=10) resorbed (FIGURE 5). During the follow-up time, no difference was found in the healing process between the groups.

Mean residual dorsal angulation in the radius was 3.4° in the BIN group and 1.4° in the ESIN group (P=0.225). In the ulna, mean dorsal angulation was 3.7° and 0.6° in these groups, respectively (P=0.022). Mean residual lateral angulation in the radius was 3.3° (BIN) and 2.09° (ESIN) (P=0.046). In the ulna, mean lateral angulation was 5.1° (BIN) and 1.6° (ESIN) (P=0.063) (Table 3).
Treatment-related findings and recovery during follow-up

The mean operation time from skin cut to complete casting was 66.9 minutes (range 18–170 min, SD 33.2 min); 80 minutes in the BIN group and 53 minutes in the ESIN group (P=0.014). A tourniquet was used in 20 cases (57.1%) according to the decision by the operating surgeon. Open reduction with a short incision at the fracture site was performed in 12 cases (34%), upon the perioperative decision by the operating surgeon in every individual case, seven of which were in the BIN group (P>0.999). All but five patients were given antibiotics; two of them were in the BIN group. Mean hospitalization time was 2.7 days in the BIN group and 2.5 days in the ESIN group (P=0.590). Above-elbow cast immobilization was carried out for every patient for 4–6 weeks, according to the study plan. No limb-length discrepancy was registered in either group.

Adverse events

There were two patients treated with BIN (2/19) vs. none treated with ESIN (0/16), who suffered re-fracture without a complete re-injury (difference 10.5%, 95% CI -10.3%–31.8%, P=0.2445) and were taken to be implant failures. A 14-year-old boy suffered from sudden pain in the forearm four weeks postoperatively. The bones were re-angulated but not displaced (FIGURE 6). A 13-year-old girl who demonstrated delayed union at follow-up suffered re-fracture three months postoperatively. No technical issues were reported in operations and primary results in both cases were good.

Drop-outs

There were two patients in the BIN group vs. none in ESIN group who suffered from a new injury resulting re-fracture and thus drop-out of follow-up (difference 10.5%, 95% CI -10.3%–31.8%, P=0.2445). Both were found to have had excellent clinical outcomes and complete union in radiographs and MRI before their new injuries. The first was a 10-year-old girl who fell from a scooter, eight months postoperatively. The other was a 9-year-old boy who was re-injured while trampolining at 10 months (FIGURE 7). The latter patient had one more fracture (distal radius) in the same forearm two months after the re-fracture. Re-fractures were fixed with plates and screws.
DISCUSSION

Forearm rotation, being the primary outcome, did not differ between all eligible patients with unstable radius- and/or ulna-shaft fractures, despite treatment with the study implant (BIN) or reference implant (ESIN) after two years’ follow-up. The patients treated with the study implant achieved a mean of 160° of pronosupination arch, which is in agreement with the rotational arch of uninjured, healthy forearms and with the gold-standard treatment ESIN. Rotational ROM was excellent also in ESIN group (mean 150°), being close to same as the ROM of nonoperatively treated forearm fractures after long-term. The majority of daily activities can be performed with 100° of forearm rotation but >30° of loss of ROM has been taken to be unsatisfactory stiffness from a clinical point of view. In this study, none of the patients showed such a decrease in either patient groups. In that regard both methods, BIN and ESIN were good at restoring the required rotational movement of forearm and may be potential treatment methods when stabilizing children’s forearm shaft fractures. The excellent rotation range is an encouraging finding, while nonsynovial joint stiffness is the most common and most important long-term complication of forearm shaft fractures. Maintenance of pronosupination is the most important goal in the management of forearm fractures. Besides, there are institutions in which the intramedullary implants are left in place. In that case the long-term modeling of the forearm may be better with BIN due to its high elasticity and resorption, in contrast to metal implants, which may affect positively on rotation capacity. However, no long-term evidence about this idea exists. In addition to forearm rotation, other important movements in elbow and wrist were analyzed as secondary outcomes and were found to be similar in both patient groups.

Three patients in the ESIN group reported some pain in the fracture area of the injured forearm after 2 years. The pain was also more usual in that group during the follow-up. According to the recommended surgical technique, titanium implants are left 4–6 mm above the bone surface, for later removal, which predisposes the patient to mechanical complications. Thus, not only pain but also discomfort from protruding nails has been reported as a potential complication of traditional ESIN. Localized pain at the implantation was not reported in either groups in this study. However, cutting the biodegradable implants at the level of the bone surface is advantageous as regards soft-tissue irritation, pain and discomfort.
Close radiographic follow-up was performed to evaluate restoration of alignment of the forearm until bone union. It has previously been determined that ≥10° of angular deformity in forearm midshaft fractures is not acceptable\textsuperscript{53,62}. The handbook of childhood fractures recommends accepting up to 15° of angulation at the midshaft level, provided the child has ≥2 years of growth remaining\textsuperscript{61,63}. In this study population, all cases treated by intra-medullary nailing achieved good alignment at two-year follow-up, regardless of the type of implant. The radius was laterally angulated at a mean of 3.3° in connection with BIN, compared with 2.1° with ESIN, which was statistically significant but far from the suggested minimal clinical significance of 10°. There was also a minor but statistically significant difference in dorsal angulation of the ulna in the BIN (3.7°) vs. ESIN (0.6°) groups, which is not clinically significant either. Principally, residual deformities such as the loss of normal radial bow may affect movements of the forearm, but the good <10° alignment after BIN is an encouraging finding, keeping in mind that biodegradable implants are less rigid than titanium nails, giving less angular support in the bones until bone union. However, due to lower elasticity, titanium nails may be preferred implants in particular for older children and adolescents with more mature bones.

There were no problems in bone healing and no nonunion was found among the patients at the two-year follow-up. Because injury and intramedullary fixation may compromise the intra-osseous circulation, midshaft forearm-shaft fractures have been considered vulnerable to nonunion. However, nonunion is uncommon\textsuperscript{64}, reported in 1-1.5% of these fractures\textsuperscript{14,65,66} and the rate of nonunion after BIN may be the same. The operation time was slightly longer in the BIN group. Reaming the medullary cavity, which is recommended prior to introduction of the study implant \textsuperscript{32}, is an extra step in the BIN procedure, compared with ESIN. Further, the technique and instrumentation were new in the institutions involved, which may have increased the operation time. The technique obviously requires more skills than traditional nailing with ESIN; therefore, we recommend BIN as a technique for surgeons familiar with childhood trauma. The hospitalization time was equal in both groups. There is no general consensus about the postoperative immobilization\textsuperscript{48} and immobilization is generally considered individually. There seems to be a trend against free mobilization after ESIN of forearm shaft by many experts. However, in this study, all the patients in both patient groups were immobilized, to standardize the study methods, according to the study plan. At the end of the follow-up period all patients could exercise at the pre-injury level and were equally satisfied with their overall results.
Two patients treated by BIN were lacking from the two-year analysis as a result of unexpected re-
displacement due to implant failure (unexpected re-fracture without a complete re-injury). There
had not been technical issues in their operations and the postoperative fracture reductions had been
good (FIGURE 4.). No particulars in their history predicted re-fracture. Despite the lack of
statistical significance, it is still possible that the failures associate with the study implant.

Nevertheless, for comparison, one in three nonoperatively treated patients needs re-reduction during
cast treatment\textsuperscript{16}, which is much more, compared with the results after both BIN and ESIN.
Unexpected re-fracture occurred in a 13-year-old adolescent girl and 14-year-old boy; perhaps they
should have been primarily considered rather like adults with a mature skeleton than children with
immature bones. For older children and adolescents the study implant may not provide enough
stability. The reason for the implant failures remains unclear, and an extended study should be
performed to refine the correct indication for BIN in children vs. adolescents and other potential
predictive factors for implant failure should be further assessed. In general, re-fracture is a known
complication of ESIN\textsuperscript{12,13,21,22,25}, and therefore the other two new fractures caused by recognized
injuries (scooter riding and trampolining) were not unexpected. Re-fracture is a reported
complication even in cases with a metallic implant remaining in the bone \textsuperscript{12,25,67-69}.

There has been an increasing trend towards operative management of long-bone shaft fractures\textsuperscript{7,70}
in recent decades. Diaphyseal fractures are characterized by limited potential for remodeling and
spontaneous correction because of the distance from the physis\textsuperscript{17}, which may justify more
aggressive surgical treatment. There are also changes is patients’ requests, economic circumstances,
living habits and sports, which may have contributed to a change against surgical fixation\textsuperscript{17}.
Biodegradable materials are of increasing interest in connection with orthopedic trauma\textsuperscript{4,23,40,71}. We
found that the study implant seemed to behave as expected, and it had mostly disappeared after two
years, allowing normal bone healing. Biodegradable implants have previously been reported to be
associated with inflammation or osteolysis\textsuperscript{42,72}, and foreign-body infections are seen in about 1–5% of patients with orthopedic implants\textsuperscript{73}. One case of deep infection was reported in the ESIN group
after implant removal, but no tissue reactions were seen in this study population. PLGA copolymers
used in BIN overcome previously reported problems related to the rapid degradation of PGA
(polyglycolic acid) material and the slow degradation of PLLA (poly-1-lactide acid) material. It
utilizes a combination of the degradation properties of both polymers\textsuperscript{74}.

This study was a pioneering prospective randomized trial about the issue, providing level-A
evidence. Most patients reached the 2-year follow-up and adverse events were analyzed in detail.
As a weakness, still longer follow-up is needed to ensure full resorption of the implants. The range of age of the patients was wide and the cases were heterogeneous in that regard. A more comprehensive study is needed to confirm appropriate patient selection in children vs adolescents. In addition, more understanding about the need for postoperative immobilization in this method should be acquired. The functional outcomes were analyzed between the two patient groups treated with the study method and reference method. To provide more detailed information about the functional outcomes in different age and patient groups, further studies should be performed with different study settings.

CONCLUSIONS

Most of the known benefits of intramedullary nailing are available with BIN, as compared with ESIN, when treating children with radius- and/or ulna-shaft fractures. The method is mini-invasive and further implant removal is not needed. However, because of the two unexpected implant failures reported in the study group, further studies are warranted for appropriate patient selection for this technique.
ACKNOWLEDGEMENTS

We are thankful to Mrs. Anna-Maija Haltia, M.Sc., and Mrs. Minna Veiranto, M.Sc., employed by Bioretec Ltd., that provided the implants for this study. We also thank The Finnish Paediatric Orthopaedics Society, the Vaasa Foundation of Physicians, The Finnish Society of Paediatric Surgeons, The Finnish Foundation of Pediatric Research and The Alma and K. A. Snellman Foundation for supporting the study.

DATA AVAILABILITY

The raw/processed data required to reproduce these findings cannot be shared at this time due to legal or ethical reasons.
REFERENCES


540 59. Flynn JM, Jones KJ, Garner MR, Goebel J. Eleven years experience in the operative

542 60. Högström H, Nilsson BE, Willner S. Correction with growth following diaphyseal forearm


545 62. Ploegmakers J, Verheyen C. Acceptance of angulation in the non-operative treatment of

547 63. Younger AS, Tredwell SJ, Mackenzie WG, Orr JD, King PM, Tennant W. Accurate prediction of

      Sep;23(5):800-4.


553 66. Sinikumpu JJ, Lautamo A, Pokka T, Serlo W. Complications and radiographic outcome of
      children's both-bone diaphyseal forearm fractures after invasive and non-invasive treatment.


Table 1. Classification of outcome of forearm-shaft fractures in children, graded using a system described by Price.\textsuperscript{53}

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Loss of Forearm Rotation and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>$\leq 15^\circ$ loss of forearm rotation and no complaints with strenuous activity</td>
</tr>
<tr>
<td>Good</td>
<td>A loss of forearm rotation of $15^\circ$ to $30^\circ$ and only mild complaints with strenuous physical activity</td>
</tr>
<tr>
<td>Fair</td>
<td>A loss of forearm rotation of $30^\circ$ to $90^\circ$ and mild complaints during activities of daily living</td>
</tr>
<tr>
<td>Poor</td>
<td>All other outcomes</td>
</tr>
</tbody>
</table>
Table 2. Radiographic bone healing of radius and/or ulna fractures two years postoperatively. Biodegradable intramedullary nailing (BIN) vs. elastic stable intramedullary nailing (ESIN).

<table>
<thead>
<tr>
<th>Fracture healing, Radius and Ulna</th>
<th>Study implant (BIN, N=15)</th>
<th>Reference implant (ESIN, N=16)</th>
<th>difference, 95% CI*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete callus in 4 cortices</td>
<td>n</td>
<td>n</td>
<td></td>
</tr>
<tr>
<td>radius</td>
<td>15</td>
<td>16</td>
<td>0 (-21 to 20)</td>
</tr>
<tr>
<td>ulna</td>
<td>14</td>
<td>14/15</td>
<td>0 (-25 to 25)</td>
</tr>
<tr>
<td>No visible fracture line</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>radius</td>
<td>15</td>
<td>16</td>
<td>0 (-21 to 20)</td>
</tr>
<tr>
<td>ulna</td>
<td>14</td>
<td>14/15</td>
<td>0 (-25 to 25)</td>
</tr>
</tbody>
</table>

*CI= confidence interval
Table 3. Residual alignment of the radius and ulna in patients with unstable childhood fractures treated by BIN vs. ESIN as measured in radiographs in anterior–posterior (AP) and lateral projections at the two-year follow-up.

<table>
<thead>
<tr>
<th>Angular deformity, degrees</th>
<th>Study implant (BIN N=15)</th>
<th>Reference implant (ESIN N=16)</th>
<th>Mean difference</th>
<th>95% CI*** of the difference</th>
<th>P-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radius, AP</td>
<td>3.4</td>
<td>1.4</td>
<td>1.9</td>
<td>-0.70-4.51</td>
<td>P=0.225</td>
</tr>
<tr>
<td>Radius, lateral</td>
<td>3.3</td>
<td>2.1</td>
<td>1.8</td>
<td>-1.35-4.95</td>
<td>P=0.046</td>
</tr>
<tr>
<td>Ulna, AP</td>
<td>3.7</td>
<td>0.6</td>
<td>4.2</td>
<td>0.96-7.49</td>
<td>P=0.022</td>
</tr>
<tr>
<td>Ulna, lateral</td>
<td>5.2</td>
<td>1.6</td>
<td>3.7</td>
<td>0.39-6.98</td>
<td>P=0.063</td>
</tr>
</tbody>
</table>

Fracture reduction

<table>
<thead>
<tr>
<th>Residual dislocation, mm</th>
<th>Study implant (BIN N=15)</th>
<th>Reference implant (ESIN N=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>radius</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ulna</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Standard deviation

**P-value measured by using independent t-tests

***95% confidence intervals
FIGURE 1

The study implant; Biodegradable intramedullary nail of poly(lactide-co-glycolide) (PLGA) with a fluoroscopy positive tricalcium-phosphate (β-TCP) marker (white arrow) in a perioperative picture while introducing the implant into radius (A) and the ulna (B).
FIGURE 2
Consolidated Standards of Reporting Trials (CONSORT) flow chart 
Thirteen patients with complete follow-up (two years) per group were required according to sample-size calculation and a total of 38 tickets (BIN, N=19 + ESIN, N=19) were randomized in sealed envelopes in advance to allow for potential loss to follow-up. However, enrolment was interrupted when the sample size was exceeded by 20% in both groups (N=16+16), with the justified expectation that a satisfactory number of cases (N>26) would complete the study. * Not recruited due to interruption of enrollment. ** Two patients suffered re-fracture without complete re-injury. *** Two patients were excluded because of new high-energy injuries.
FIGURE 3
The angulation was determined by drawing the lines align with the axis of both bone fragments (straight black lines) and the angle between the two lines was then calculated.
FIGURE 4
A 9-year-old boy fell from a trampoline, fracturing both forearm bones (A, B). The fractures were closed and surgically stabilized by means of biodegradable elastic stable intramedullary nailing (BIN). The nails are invisible in postoperative radiographs (C, D), but the tricalcium phosphate markers in the tips of the nails can be seen (arrows). After two years the bones were completely united and in good alignment (E, F).
FIGURE 5
T2-weighted magnetic resonance images with axial projections of a forearm-shaft fracture, treated by means of BIN demonstrated the biodegrading process of the polylactide-co-glycolide nails. The nails (white arrows) were sharp-edged and intact at one month of follow-up but edema was seen in the soft-tissue surroundings (A). The nails were still intact after 3 months (B) and 12 months (C). Two-year follow-up MRI demonstrated low-signal nails that were irregular and had partly disappeared (*). No soft-tissue edema remained at two years.
Two patients treated with the study implants (BIN) suffered from sudden implant failure without a new injury. The first was a boy aged 14 years (A, B) who was appropriately stabilized with two intramedullary nails (C, D; postoperative radiographs). The patient felt sudden pain and the bones were found to be angulated at 4 weeks follow-up (E, F).

Another patient, a 13 years old girl, had suffered from an unstable diaphyseal forearm fracture (G, H). She was appropriately treated by means of BIN (I, J). At 3 months follow-up visit the bones were found to be angulated (K, L). Both were stabilized with plate fixation. These patients were not considered in the two-year follow-up.
There were two BIN patients who suffered new injuries during follow-up. The first was a girl aged 10 years (A, B) who was appropriately stabilized with two intramedullary nails (C, D; postoperative radiographs). At six months, the bones were united in good alignment (E, F). Eight months after the first injury, the patient fell when riding a scooter and suffered a re-fracture. Another patient, a boy aged eight, had suffered from an unstable diaphyseal forearm fracture (I, J). He was appropriately treated by means of BIN (K, L) and bone union was good at the six-month follow-up (M, N). Unfortunately, the patient fell while trampolining, suffering a new fracture in the radius (O, P). These patients were not considered in the two-year follow-up.