



Hydroxyapatite pins for external fixation: is there sufficient evidence to prove that coated pins are less likely to be replaced prematurely?

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Objective: Several clinical studies have reported that the use of hydroxyapatite- (HA) coated pins enhance external fixation. Although these studies have demonstrated higher extraction torques and lower rates of pin loosening with HA coating, there is little evidence to suggest that these biomechanical advantages translate to a lower rate of pin replacement prior to healing. The research question posed was “Is there sufficient evidence to prove that hydroxyapatite coating lowers the rate of pin replacement for external fixation?”

Methods: An electronic search of Medline (Ovid, 1946 - December Week 4 2011), Embase (Ovid, 1980—2011 Week 52), and the Cochrane Central Register of Controlled Trials (Issue 4 of 4, October 2011) was conducted to identify all randomized and quasi-randomized controlled trials which compared HA-coated pins with non-coated pins for external fixation, with particular emphasis on the premature replacement of pins as a consequence of loosening.

Results: The combined search strategies retrieved 72 citations. Four randomized controlled trials (101 patients, 327 HA-coated vs. 354 uncoated pins) were included in this review. None of the studies demonstrated a clear benefit between pin types with respect to premature replacement of pins prior to healing.

Conclusion: This review did not find sufficient evidence to validate the preferential use of HA-coated pins over standard pins as a means of avoiding premature replacement of pins used for external fixation. The use of uncoated pins is justifiable, especially within the context of limited financial resources.

Keywords: External fixation; hydroxyapatite; systematic review.

External fixators are external devices which hold wires or pins that are placed through 1 or both cortices of bone in order to maintain the proper alignment of a fracture. These devices offer relative advantages such as greater access to wounds, adjustment during the course of bone healing, and more functional use of the limbs involved.

Relevant clinical applications include tentative or definitive treatment of fractures, deformity corrections, limb lengthening and treatment of non-unions.^[1]

The bone-pin interface is the point of contact between the bone and the pins or wires of the external fixation system. This interface transmits loads from the

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bone to the external fixator and plays a vital role in the mechanical stability of the construct. The biomechanical integrity of the interface depends on several factors, including pin insertion technique, fibrous tissue formation, mechanical loading, dynamization, preloading, and the presence or absence of coating.^[2] Pins coated with hydroxyapatite (HA) have been developed to improve the direct structural and functional connection between living bone and implants (osteointegration).^[3]

Several clinical studies have reported that HA-coated pins enhance fixation when used for external fixation.^[2,4] Although these studies have demonstrated relatively higher extraction torques and lower rates of pin loosening and pin track infections with HA-coated pins, none of these studies have proven that these advantages translate to a reduction in the replacement of pins prior to union.

The aim of this systematic review was to address the pertinent research question, "Is there sufficient evidence to prove that hydroxyapatite coating lowers the rate of premature pin replacement for external fixation?"

Materials and methods

This review includes all randomized and quasi-randomized controlled trials which compared HA-coated pins with non-coated pins for external fixation, with emphasis on premature pin replacement prior to union.

Study participants consisted of children and adults who had received treatment with external fixation for at least 3 months regardless of the indication (definitive treatment of long bone fractures, osteotomies, limb deformity correction, non-unions, etc.).

Eligible studies made direct comparisons between HA-coated and non-coated pins made of the same material, e.g. HA-coated steel vs. uncoated steel. The primary outcome measure of interest was the premature replacement of pins as a consequence of loosening.

An electronic search of MEDLINE (Ovid, 1946-December Week 4 2011), Embase (Ovid, 1980—2011 Week 52), and the Cochrane Central Register of Controlled Trials (Issue 4 of 4, October 2011) was conducted on the 28th of December 2011. A detailed outline of the MEDLINE and Embase search strategy is shown in Appendices 1 and 2. The electronic search was complemented by a manual search through the bibliographies of retrieved articles. There were no language restrictions.

The search results from the electronic search strategy were merged using Endnote reference management software (Thomson Reuters, Philadelphia, PA, USA). Duplicate records of the same report were eliminated. Titles and abstracts of all citations were examined indepen-

dently against the eligibility criteria by both review authors. Full text articles of potentially eligible studies were retrieved and assessed independently by the authors. Disagreements were resolved by discussion. All studies that fulfilled the inclusion criteria were included in this review.

The risk of bias of the included studies was assessed with the Cochrane Collaboration's tool for assessing risk of bias.^[5] The tool assesses the risk of bias across 6 major domains: sequence generation, allocation concealment, blinding of participants, incomplete outcome data, selective outcome reporting, and other sources of bias.

Results

The combined search strategies retrieved 72 citations. Ten studies were potentially relevant, as they involved the use of HA-coated pins within the context of external fixation.^[4,6–15] Review of the full text of these studies led to 6 further exclusion: 2 randomized controlled trials that involved the use of HA-coated pins for less than 3 months,^[8,9] a study based on comparisons between titanium and steel pins,^[12] a duplicate study,^[6] a systematic review,^[10] and a trial with irrelevant outcome measures.^[13] At the end of the screening process, 4 studies were included in this review.^[4,7,14,15]

Magyar 1997: Magyar and colleagues conducted a multicenter randomized controlled trial designed to compare standard tapered pins (Orthofix 6/5 mm) to similar pins with HA coating in 19 patients (mean age: 54 years; range: 38–75 years) treated with hemicallosis for medial compartment knee osteoarthritis. The authors did not provide sufficient evidence regarding the selection process to validate the study cohort as an unbiased representation of the eligible population. Allocations to interventions were concealed in numbered, sealed, envelopes. The risk of selection bias was unclear.

The surgical technique was explicitly documented. All but 1 patient had the Orthofix T-garthe frame secured exclusively with 4 coated or 4 uncoated 6/5 mm tapered pins. Pre-drilling of the metaphyseal and cortical bone was done to facilitate insertion of both pin types. The osteotomy was performed at the level of the distal third of the tibial tuberosity, and the mean fixation time was 101 days. There was no evidence to suggest that blinding, wherever practical, was performed in any facet of the intervention or the assessment of outcomes. The risk of performance and detection bias was adjudged as high.

There were no reported cases of premature replacement of pins. However, there was a statistically significant difference ($p < 0.005$) in extraction torque forces, as the HA-coated pins seemingly enhanced fixation. All

pins were accounted for in the analysis, and the most relevant outcomes were reported. The risk of attrition and reporting bias was adjudged as low.

Moroni 1998: Moroni recruited 21 consecutive participants treated with external fixation for mid-diaphyseal fractures of the tibia. Eligible patients were between the ages of 15 and 55 years and had closed or Gustilo type I open fractures. Allocation to 1 of 3 groups (apex uncoated pins, superfixation bicylindrical uncoated pins, superfixation bicylindrical HA-coated pins) was guided by a computer-generated sequence. There were no documented attempts to conceal allocations, hence the risk of selection bias was adjudged as unclear.

All fractures were stabilized with 6 self-drilling, self-tapping pins (3 proximal and 3 distal to the fracture site) secured to either a Hoffman unilateral external fixator (apex group; frame stiffness: 800 N/cm) or a Star 90 (Citieffe; Bologna, Italy) unilateral external fixator (bicylindrical uncoated and bicylindrical HA groups; frame stiffness: 1037 N/cm). All pins were inserted manually, although the coated pins were implanted after predrilling. Postoperative weight bearing, dynamization, and removal of the external fixator were tailored according to individual needs as adjudged by the principal investigator. Overall, there were notable differences in various facets of the intervention that may have introduced a systematic performance bias. Furthermore, there was no evidence to suggest that blinding, wherever practical, was performed in any facet of the intervention or the assessment of outcomes.

There were no reported incidents of pin replacement prior to healing across the 3 groups. The median extraction torque was significantly higher in the HA-coated pins (2.1 Nm) compared to that of their uncoated counterparts (both 0.1 Nm). There were no reported losses to follow-up, and relevant outcomes were reported, minimizing the risk of attrition and selective reporting bias.

Moroni 2001: Moroni^[4] enrolled 38 consecutive patients (157 pins) who had external fixation of the femur or tibia for fracture fixations, bone transport, and osteotomies across 3 centers. Patients were allocated to treatment with external fixation using either tapered stainless steel 6/5 mm standard pins or HA-coated equivalents based on a computer-generated sequence. The authors did not provide adequate information about the methodological rigor of the selection process or attempts to conceal allocations, hence the risk of selection bias was adjudged as unclear.

Eighteen patients (71 pins) were allocated to the uncoated group, with a standard unilateral fixator mounted

in 15 patients and a hybrid circular frame utilized in 3 patients. The 20 patients (86 pins) assigned to the HA group had a unilateral fixator in 16 patients and a hybrid fixator in the remaining 4. All pins were inserted manually after predrilling (3.2 mm drill in cancellous bone, 4.8 mm drill in cortical bone). Postoperative weight bearing and removal of the external fixator were tailored according to individual needs as adjudged by the principal investigator in each center. There were no reported attempts to blind, hence there was inherent risk of performance bias.

There were no reported cases of pin replacement as a consequence of loosening over the mean implantation time of 147 days in the uncoated group and 186 days in the HA-coated group. Mean extraction torque was lower for standard pins than for the HA-coated pins ($p < 0.001$). There were no reported attritions or loss to follow-up.

Piza 2004: Piza^[7] and colleagues prospectively enrolled 23 pediatric patients (12 boys, 11 girls; mean age: 12.7 years) who required 28 bilateral limb lengthenings for short stature. HA-coated tapered stainless steel 6/5 mm pins were implanted in 1 limb and identical uncoated pins in the other based on random assignments by a preoperative coin toss. The authors did not provide adequate information about the robustness of the selection process, and the adopted treatment allocation method does not lend itself to adequate concealment.

The pin insertion and surgical lengthening techniques were performed in accordance with standardized published methods. Of 23 patients, 17 had tibial lengthening, 4 had simultaneous femoral and humeral lengthening, 1 had femoral lengthening, and 1 had simultaneous humeral and tibial lengthening. Overall, 322 pins were implanted (161 of each pin type). Postoperative rehabilitation was tailored according to the individual, and the lengtheners were removed based on explicitly defined radiological criteria. There were no reported attempts to blind any facet of the intervention or assessment of outcomes.

The authors reported that 19 pins were removed before bone healing due to evident loosening (mean duration of implantation: 530 ± 167 days) without a statistically significant difference between the 2 groups. The mean extraction torques were significantly higher in the HA-coated group ($p < 0.001$). The authors observed that loosening, defined as an extraction torque of ≤ 150 Nmm degrees⁻¹, occurred in 4% of HA-coated pins and 80% of uncoated pins ($p < 0.001$). There was no reported loss to follow-up or evidence of selective outcome reporting.

A summary of the included study characteristics and risk of bias is highlighted in Tables 1 and 2 below.

Table 1. Descriptive summary of included studies.

Study	Participants	Intervention(S)	Outcomes	Results
Magyar et al. 1997	19 patients (76 pins) Mean age: 54 years (38–75) Hemicallotasis (Knee OA) Orthofix 6/5 mm vs. HA 6/5 mm	Hemicallotasis steotomy 2 metaphyseal + 2 diaphyseal pins *Exclusive HA /uncoated pins + anterior external fixator Predrilling for both pin types Mean fixation time: 101 days (range: 61–155 days)	Mean insertion and extraction torques, **Pain (VAS)	No pins replaced *Higher extraction torques in HA Group (p<0.005) No statistically significant difference in insertion torques
Moroni et al. 1998 Multicenter RCT	21 patients (126 pins) Age: >15 years<55 years Tibial shaft fractures (Closed or Gustilo type I) Computer-generated sequence	Apex vs. bicylindrical vs. bicylindrical HA (5 mm SS vs. 4–5 mm SS vs. HA 4–5 mm) 3 pins proximal, 3 pins distal to fracture + Hoffman or Star 90 unilateral ext fix Differences in pin insertion techniques and frames across groups	Mean insertion and extraction torques, radiolucency, mechanical loosening, pin tract infections	No pins replaced *Higher extraction torques in HA Group (p<0.001) *No significant difference in median insertion torque *Higher pin tract infections in pooled uncoated vs HA group (p<0.03)
Moroni et al. 2001 Multicenter RCT	38 patients (157 pins) Mean age: 48 years (HA), 49 years (S) Mixed cohort: fractures, bone transport, osteotomies Computer-generated sequence	6/5 mm HA vs. standard pins Mostly unilateral frames Predrilling for both pin types Manual insertion Mean fixation time: 147 days (S), 186 days (HA)	Mean insertion and extraction, torques	No pins replaced *Higher extraction torques in HA group (p<0.001) *Higher pin tract infections in uncoated group(p<0.009)
Piza et al. 2004 Multicenter RCT	23 Patients (322 pins) Mean age: 12.7 years Leg lengthening Coin toss allocation for treatment	6/5 mm HA vs. standard pins Orthofix lengthener Complex spectrum of soft tissue interventions Mean fixation time: 512 days (S), 549 (HA)	Replaced pins, extraction and insertion torques	13 pins replaced HA (6 pins), uncoated (13) *No statistically significant difference between groups

*One patient had a mixture of coated and HA-coated Pins (2 each). ** VAS: Visual analog scale; SS: Stainless steel; (S): Standard (HA) coated group.

Table 2. Summary of risk of bias of included studies.

	Selection bias	Performance bias	Detection bias	Attrition bias	Selective reporting bias
Magyar et al. 1997	?	+	+	-	-
Moroni et al. 1998	?	+	+	-	-
Moroni et al. 2001	?	+	+	-	-
Piza et al. 2004	+	+	+	-	-

+: High risk; -: Low risk; ?: Unclear risk.

Discussion

The aim of this systematic review was to compare the efficacy of HA-coated pins with that of uncoated pins

when used for external fixation with respect to the need for replacement of pins prior to healing.

Four randomized controlled trials (101 patients, 327

HA-coated vs. 354 uncoated pins) were included in this review.^[4,7,14,15] None of the studies demonstrated that HA coating reduced or eliminated the need for replacement of pins prior to healing relative to its uncoated counterpart. No pins were replaced in 3^[4,14,15] of the 4 included studies, although the authors reported significantly lower extraction torques relative to uncoated pins. In the only trial^[7] in which pins were replaced, there was no statistically significant difference between the coated and uncoated groups. The absence or relatively small number of pins replaced across the studies over a mean implantation time of 3–18 months suggests that clinically significant pin loosening in external fixation is rare or perhaps well tolerated in the acute context. In a previous review,^[10] the data needed to avoid clinically significant loosening could not be determined due to the relatively small number of primary studies that reported premature pin replacement.

The decision to replace pins is multifactorial, considering aspects such as pin insertion technique, fibrous tissue formation, mechanical loading, dynamization, preloading, infection, and patient compliance. The surgeon's discretion also plays a significant role in the decision for and timing of pin replacement. None of the included studies set explicit criteria for pin replacement at any stage of healing. The measurement of extraction torques was done at the time of removal of the fixators. Subsequent categorization of pins as "loose" at that stage would appear irrelevant, having served their purpose throughout the duration of healing. In clinical practice, the decision to replace pins prior to healing is more likely to be based on clinical judgement rather than routine outpatient measurement of extraction torques, which may be more objective.

Two of the 4 included studies^[4,14] reported statistically lower pin tract infections in the HA-coated group. Notably, this advantage did not translate to a difference in the rate of pin replacement prior to healing, as no pin was replaced prematurely in either study. In the other 2 studies, including the limb lengthening study^[7] with the largest number of pins and longest implantation period (over 530 days), there was no statistically significant difference in the incidence of pin tract infection between the 2 groups. The ability to protect against clinically significant infection was not consistently reproducible across studies. This may be related to other confounders such as pin insertion technique and soft tissue envelopes that varied across studies.

The methodological strength of the included studies centered on a relatively low risk of attrition and selective reporting biases. However, confidence in the integrity

of the selection process, concealment of allocation, and blinding was limited by the quality of reporting and attempts to blind across all trials. Overall, caution must be exercised in the interpretation of the results and, hence, ramifications to clinical practice.

In conclusion, this review has not found sufficient evidence to validate the preferential use of HA-coated pins over standard pins as a means of avoiding premature replacement of pins used for external fixation. The use of uncoated pins is justifiable, especially within the context of limited financial resources. Further adequately powered well designed randomized controlled trials are required to validate the optimal benefit of HA-coated pins.

Conflicts of Interest: No conflicts declared.

References

1. <http://www.ncbi.nlm.nih.gov/mesh> (accessed 20th of April/2012).
2. Moroni A, Vannini F, Mosca M, Giannini S. State of the art review: techniques to avoid pin loosening and infection in external fixation. *J Orthop Trauma* 2002;16:189–95.
3. Carlos JL, Carneiro J. Inorganic matter represents about 50% of the dry weight of bone. In: Boyle P, editor. *Basic Histology, Text & Atlas*. 10th ed. McGraw-Hill Companies; 2003.
4. Moroni A, Heikkilä J, Magyar G, Toksvig-Larsen S, Giannini S. Fixation strength and pin tract infection of hydroxyapatite-coated tapered pins. *Clin Orthop Relat Res* 2001;388:209–17.
5. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
6. Caja VL, Pizà G, Navarro A. Hydroxyapatite coating of external fixation pins to decrease axial deformity during tibial lengthening for short stature. *J Bone Joint Surg Am* 2003;85-A:1527–31.
7. Pizà G, Caja VL, González-Viejo MA, Navarro A. Hydroxyapatite-coated external-fixation pins. The effect on pin loosening and pin-track infection in leg lengthening for short stature. *J Bone Joint Surg Br* 2004;86:892–7.
8. Pieske O, Kaltenhauser F, Pichlmaier L, Schramm N, Trentzsch H, Löffler T, et al. Clinical benefit of hydroxyapatite-coated pins compared with stainless steel pins in external fixation at the wrist: a randomised prospective study. *Injury* 2010;41:1031–6.
9. Pieske O, Pichlmaier L, Kaltenhauser F, Schramm N, Rubenbauer B, Greiner A, et al. Hydroxyapatite-coated pins versus titanium alloy pins in external fixation at the wrist: a controlled cohort study. *J Trauma* 2011;70:845–51.
10. Saithna A. The influence of hydroxyapatite coating of ex-

ternal fixator pins on pin loosening and pin track infection: a systematic review. *Injury* 2010;41:128–32.

11. Sandén B, Olerud C, Petré-Mallmin M, Larsson S. Hydroxyapatite coating improves fixation of pedicle screws. A clinical study. *J Bone Joint Surg Br* 2002;84:387–91.
12. Pommer A, Muhr G, Dávid A. Hydroxyapatite-coated Schanz pins in external fixators used for distraction osteogenesis: a randomized, controlled trial. *J Bone Joint Surg Am* 2002;84-A:1162–6.
13. Campbell AA, Song L, Li XS, Nelson BJ, Bottoni C,

Brooks DE, et al. Development, characterization, and anti-microbial efficacy of hydroxyapatite-chlorhexidine coatings produced by surface-induced mineralization. *J Biomed Mater Res* 2000;53:400–7.

14. Moroni A, Aspenberg P, Toksvig-Larsen S, Falzarano G, Giannini S. Enhanced fixation with hydroxyapatite coated pins. *Clin Orthop Relat Res* 1998;346:171–7.
15. Magyar G, Toksvig-Larsen S, Moroni A. Hydroxyapatite coating of threaded pins enhances fixation. *J Bone Joint Surg Br* 1997;79:487–9.

Appendix 1. MEDLINE search strategy.

# ▲	Searches	Results
1	Exp external fixators	4304
2	Exp bone nails/	8171
3	Exp bone screws/	14805
4	Exp bone wires/	4232
5	(External adj [fixat\$ or pins\$ or wires\$ or nail\$ or rods\$]).mp.	7448
6	Skeletal traction.mp.	514
7	Steinmann pin\$.mp.	250
8	1, 2, 3, 4, 5, 6, 7	31362
9	Exp durapatite/	9453
10	Hydroxyapatite.mp.	13965
11	9, 10	16804
12	Randomized controlled trial.pt.	315877
13	Controlled clinical trial.pt.	83182
14	Randomized.ab.	221432
15	Placebo.ab.	127183
16	Drug therapy.fs.	1488786
17	Randomly.ab.	160369
18	Trial.ab.	228368
19	Groups.ab.	1061229
20	12, 13, 14, 15, 16, 17, 18, 19	2757907
21	Exp animals / not humans.sh.	3639193
22	20 not 21	2340745
23	8 and 11 and 22	49

Appendix 2. Embase search strategy.

	Searches	Results
1	Exp external fixator/	4374
2	Exp bone screw/	15160
3	Exp Kirschner wire/	4306
4	Exp bone nail/	8311
5	(External adj [fixat\$ or wires\$ or rods\$ or pin\$ or nail\$]).ti,ab.	5857
6	1, 2, 3, 4, 5	31512
7	Exp hydroxyapatite/	9649
8	Hydroxyapatite.mp.	14237
9	7, 8	17108
10	Exp randomized controlled trial/	324772
11	Exp double blind procedure/	0
12	Exp single blind procedure/	0
13	Exp crossover procedure/	0
14	10, 11, 12, 13	324772
15	Animal/ not human/	3611730
16	14 not 15	318784
17	6 and 9 and 16	24