Osteointegration of hydroxyapatite-coated collars in cemented massive endoprostheses following revision surgery

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Aims
Hydroxyapatite (HA)-coated collars have been shown to reduce aseptic loosening of massive endoprostheses following primary surgery. Limited information exists about their effectiveness in revision surgery. The aim of this study was to radiologically assess osteointegration to HA-coated collars of cemented massive endoprostheses following revision surgery.

Methods
Retrospective review of osseointegration frequency, pattern, and timing to a specific HA-coated collar on massive endoprostheses used in revision surgery at our tertiary referral centre between 2010 to 2017 was undertaken. Osseointegration was radiologically classified on cases with a minimum follow-up of six months.

Results
In all, 39 patients underwent radiological review at mean 43.5 months; 22/39 (56.4%) showed no osseointegration to the collar. Revision endoprostheses for aseptic loosening were less likely to show osseointegration compared with other indications for revision. Oncological cases with previous or current infection were more likely to show osseointegration to ≥ 1 collar side than those without evidence of prior infection.

Conclusion
This seven-year review identified osseointegration of HA-coated collars after revision surgery is less likely (43.6%, 17/39) than after primary surgery. Young patients who undergo revision surgery following initial oncological indication may benefit the most from this collar design. Use in revision oncological cases with a history of infection may be beneficial. HA-coated collars showed limited benefit for patients undergoing revision for failed arthroplasty with history of infection.

Cite this article: Bone Jt Open 2021;2-6:371–379.

Keywords: Hydroxyapatite, Osteointegration, Joint Reconstruction, Bone Tumour, Sarcoma, Massive Endoprosthesis

Introduction
Massive endoprosthetic arthroplasty is a well-established method of limb reconstruction in orthopaedic oncology after tumour resection, and for complex revision arthroplasty. In revision surgery, the biological environment may influence outcomes and make reconstructive surgery challenging. Aseptic loosening is the most common indication for revision surgery after cemented and uncemented massive endoprosthetic reconstruction, reported in up to 35% of primary distal femoral arthroplasties over four to ten years, and up to 46% of proximal tibial arthroplasties. It is likely a consequence of cortical bone loss at the bone-implant interface, followed by progressive osteolysis along the implant stem as a result of mechanical forces through it.

Previous studies have shown that when osseointegration occurs implants are less likely to show failure, especially aseptic loosening. Hydroxyapatite (HA) is an osteoconductive agent, usually plasma coated in a thin layer onto orthopaedic implants to...
promote bone on-growth. HA-coated collars have been used on massive endoprosthetic arthroplasties since 1992 to encourage extracortical bone growth, bone bridging and osseointegration, and reduce the development of radiolucent lines around the cemented stem associated with loosening.\textsuperscript{3,8,9,11} Extra-cortical bone-bridging and osseointegration at the bone-collar interface may improve the transfer of mechanical forces between implant and bone, reducing load on the stem and cement mantle thereby reducing mechanical loosening.\textsuperscript{3,11,17-20} Extra-cortical bone fixation to the implant may also prevent aseptic loosening by creating a “biological purse string”, a physical barrier preventing migration of wear particles and associated osteolysis.\textsuperscript{21}

Osseointegration to HA-coated collars varies after primary endoprosthetic implantation. Between 65% to 81% of implants show osseointegration on ≥ 1 collar side over two to 18 years.\textsuperscript{3,11} Where osseointegration is seen on ≥ 1 side of the HA-coated collar in primary endoprosthetic implantation, implant survival can be up to 98% at ten years.\textsuperscript{8,11} Failure of primary surgery is influenced by differences in biological environments such as infection, periprosthetic bone loss, and implant loosening. These factors may influence osseointegration following revision surgery.\textsuperscript{1,2,6}

Clinical experience at our tertiary referral centre suggested osseointegration to the HA-coated collar was less likely after revision than primary surgery. To date, no studies are available that have investigated the outcomes of the use of massive endoprosthesis with HA-coated collars in revision surgery. This likely reflects the limited number of specialist centres that undertake high volume complex revision surgery. Additionally, no previous studies have reported at what time postoperative osseointegration first occurs.

The aim of this study was to radiologically assess osseointegration at HA-coated collars of cemented massive endoprostheses following revision surgery, and to determine if specific clinical factors influenced outcomes. Additionally, to determine at what time point postoperatively osseointegration starts to occur.

**Methods**

This single-centre, retrospective cohort review identified patients using the hospital (Royal National Orthopaedic Hospital, Stanmore, UK) coding system as having undergone further revision at study conclusion. All cases were performed by a group of five orthopaedic oncology surgeons with over ten years experience of using revision endoprostheses. All cases involved bone resection using an oscillating saw without attempt to preserve a periosteal sleeve to reattach to the HA-collar and without irrigation. No additional osteoconductive agents were used at the bone-collar interface. The collar is sized to match the bone at time of surgery.

Clinical characteristics obtained from records were: date and indication for primary procedure; indication for revision; number of procedures at that anatomical site; type of endoprostheses implanted for revision; evidence of previous or current infection based upon microbiological investigation of five or more deep tissue samples taken at time of revision surgery; age; smoking status; chemotherapy; and local radiotherapy.

Indication for revisions were classified into: aseptic loosening (loose implant without clinical or microbiological evidence of infection); infection (clinical or microbiological evidence of periprosthetic infection); implant failure (broken implant, linkage failure or failure/end point of growing mechanism); and periprosthetic fracture (fracture around implant without failure of endoprosthesis).

Two out of three clinicians (BD, LA, RK) independently reviewed the plain radiographs, with disagreements resolved by consensus. Osseointegration was defined as the presence of extrasseous bone growth overlying the HA-coated collar without a radiolucent line between the new bone growth and the collar. Osseointegration at the HA-collar was classified by two methods:

1. Zone score\textsuperscript{11} – osseointegration scored 0 to 4, according to the number of bone-collar junctions where osseointegration was seen (up to 2 on AP and 2 on lateral films).
2. Ongrowth grading\textsuperscript{22} – osseointegration graded according to the method shown in Figure 1.

Both grade 1 and 2 represent failure to osteointegrate to the HA-coated collar. Serial postoperative radiographs were reviewed to identify at what time osseointegration first occurred.

Outcomes collected were compared against the outcomes for primary endoprosthetic implantations reported in the literature. Articles were identified using keywords (“osseointegration” OR “osseointegration” AND “massive endoprosthesis”) in PubMed. Relevant articles were identified and hand searching references of these identified further relevant articles.

**Statistical analysis.** Univariate logistic regression was performed for ongrowth (no on-growth vs ≥ 1 side of osseointegration) and ordinal logistic regression for time to osseointegration first seen (Stata v15; StataCorp, USA) testing the predictive value of recorded clinical factors.
An unpaired t-test was used to determine demographic differences between subgroups for analysis. A p-value < 0.05 was considered statistically significant.

The project was reviewed by the institute research review panel and concluded that it did not require approval from a Research Ethics Committee.

**Results**

In all, 39 patients met the inclusion criteria. Mean patient age at time of revision surgery was 42.7 years (5 to 89). Mean follow-up was 43.5 months (8 to 94). The indication for the primary procedure was oncological in 32/39 patients (82.1%) and non-oncological in 7/39 (18.0%). Patient demographics, tumour type for oncological cases, endoprosthesis implanted, and indication for revision are summarized in Table I. Of note, revision of the diaphyseal arthroplasty was associated with change of only one HA-coated collar-stem component.

In 17 patients (43.6%), it was the first revision of the endoprosthesis. In the non-oncological cohort, all cases had received at least two previous revision operations. Patients in the non-oncological group were significantly older than the oncological group (mean 70.7 years vs 36.5 years; p < 0.001). No patients in the non-oncological group were aged < 40 years.

**Osseointegration.** Overall, 22 (56.4%) implants showed no osseointegration to any side of the collar. Of these, 16/22 (72.7%) showed a grade 2 pattern of growth (Figures 1 and 2).

The mean time to first radiological osseointegration seen was 13 months postoperatively, with the earliest at five months (5 to 45; Figure 3). Two patients had follow-up less than 12 months, and both showed osseointegration to ≥1 collar side. The patient showing first osseointegration at 45 months had no radiographs between 21 to 45 months postoperatively.

There was no difference in the follow-up of the patients who did and did not show osseointegration (46 vs 41.5 months; p = 0.547).

**Indication.** Patients undergoing revision for aseptic loosening were less likely to show osseointegration (4/15, 26.7%) than cases revised for other indications (Table II). These differences were not statistically significant.

In the failed arthroplasty cohort, only 1/7 (14.2%) showed osseointegration to one side of the collar, and none on more than one side, while 16/32 (50.0%) having revision of an implant originally implanted for oncological indications had osseointegration on ≥1 collar side (odds ratio (OR) 6.82; p = 0.12) (Table II).

**History of infection.** Cases were stratified into three groups based on history of implant site infection: failed arthroplasty cases with history of infection (n = 7, 17.9%), all of the failed arthroplasty cohort), oncological cases with history of infection (n = 11, 28.2%), and oncological cases with no previous infection (n = 21, 53.8%).

Osseointegration to ≥1 collar side was found to be most frequent (72.7%, 8/11) in the oncological cases with a history of infection. They were more likely to show osseointegration compared to the oncological cases without history of infection (38.1%, 8/21; OR 4.33, p = 0.071) and significantly so, compared to failed arthroplasty cases (14.3%, 1/7; OR 16, p = 0.030) (Table II).

**Age.** Patients aged below the median age of cohort (≤39 years) more frequently demonstrated osseointegration on ≥1 side of the HA-coated collar (55.0% (11/20) vs 31.6% 6/19); p = 0.145) (Figure 4a). Of patients age ≥40

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Fig. 1
AP and lateral plain radiographs representing the four grades of growth: a) Grade 1: No osseointegration or bone growth. b) Grade 2: Bone growth around collar with gap between new bone and collar. c) Grade 3: Osseointegration in 1 or 2 zones. d) Grade 4: Osseointegration in 3 or 4 zones.
Table I. Patient demographics.

| Indication                        | Total, n (%) | Mean age at time of revision (range) | Osteo-integration to ≥ 1 side of collar, n (%) | Sex, n (%) | Prosthesis, n (%) | Indication for revision, n (%) |
|-----------------------------------|--------------|--------------------------------------|-----------------------------------------------|------------|------------------|-------------------------------|
|                                   |              | M 35 (50.0)                          | F                                             | PFA        | DFA              | PTA              | TDA              | Aseptic loosening | Infection | Implant failure | Periprosthetic fracture |
| Oncological                       | 32 (82.1)    | 16 (50.0)                            | 13 (40.6)                                     | 19 (59.4)  | 8 (25.0)         | 19 (59.4)        | 4 (12.5)         | 1 (3.1)          | 13 (40.6) | 10 (31.3) | 5 (15.6) | 4 (12.5) |
| Osteosarcoma                      | 14 (35.9)    | 6 (42.9)                             | 4 (28.6)                                      | 10 (74.0)  | 1 (7.1)          | 9 (64.3)         | 3 (21.4)         | 1 (7.1)          | 5 (35.7) | 3 (21.4) | 4 (28.6) | 2 (14.3) |
| Chondrosarcoma                    | 3 (7.7)      | 1 (33.3)                             | 2 (66.7)                                      | 1 (33.3)   | 1 (33.3)         | 2 (66.7)         | 0 (0.0)          | 0 (0.0)          | 1 (33.3) | 1 (33.3) | 0 (0.0)  | 1 (33.3) |
| Giant cell tumour of bone         | 6 (15.4)     | 3 (50.0)                             | 4 (66.7)                                      | 2 (33.3)   | 1 (16.7)         | 4 (66.7)         | 1 (16.7)         | 0 (0.0)          | 3 (50.0) | 2 (33.3) | 1 (16.7) | 0 (0.0)  |
| Metastatic disease                | 2 (5.1)      | 2 (100)                              | 0 (0.0)                                       | 2 (100)    | 0 (0.0)          | 0 (0.0)          | 0 (0.0)          | 1 (50.0)         | 0 (0.0)  | 0 (0.0)  | 1 (50.0) |
| Non-osteogenic spindle cell sarcoma | 7 (18.0)   | 4 (57.1)                             | 1 (14.3)                                      | 6 (85.7)   | 3 (42.9)         | 4 (57.1)         | 0 (0.0)          | 0 (0.0)          | 3 (42.9) | 1 (57.1) | 0 (0.0)  | 0 (0.0)  |
| Failed arthroplasty               | 7 (18.0)     | 1 (14.3)                             | 3 (42.9)                                      | 4 (57.1)   | 2 (28.6)         | 5 (71.4)         | 0 (0.0)          | 0 (0.0)          | 2 (28.6) | 2 (28.6) | 2 (14.3) | 1 (28.6) |
| Overall                           | 39           | 17 (43.6)                            | 16 (41.0)                                     | 23 (59.0)  | 10 (25.6)        | 24 (61.5)        | 4 (10.3)         | 1 (2.6)          | 15 (38.5) | 12 (30.8) | 7 (18.0) | 5 (12.8) |

DFA, distal femoral arthroplasty; PFA, proximal femoral arthroplasty; PTA, proximal tibial arthroplasty; TDA, tibial diaphyseal arthroplasty.
years without osseointegration, 11/13 (84.6%) showed grade 2 pattern of growth compared to 6/11 (54.5%) in those ≤ 39 years (Figure 4b).

In the patients aged < 40 years, all of whom underwent primary surgery for oncological indications, those revised for aseptic loosening were less likely to show osseointegration (28.5%, 2/7) compared to those revised for infection (83.3%, 5/6; OR 12.5, p = 0.067).

Clinical characteristics. Smoking status, number of previous operations, and previous chemotherapy and/or radiotherapy, did not show statistical significance for osseointegration to ≥ 1 collar side (Table II) or for osseointegration grade.

Patients undergoing a primary revision showed no statistically significant difference in osseointegration to ≥ 1 collar side (7/17, 41.2%) compared to those having undergone multiple revisions (10/22, 45.6%) (OR 1.19 (95% confidence interval (CI) 0.33 to 4.28), p = 0.789). Greater frequency of osseointegration was seen more than five years after implantation (71.4% (5/7) vs 37.5% (12/32)).

Anatomical location of implant. Comparing PFAs and DFAs, there was no significant difference in the frequency of osseointegration (Table II), or in the anatomical aspect of the collar where growth occurred.

Time to osseointegration. No specific clinical factors showed statistical significance for effect on time to first osseointegration seen (Table II). Mean time for PFAs to osteointegrate (9.8 months; 5 to 21) tended to be earlier than DFAs (14.7 months, 6 to 45; p = 0.125). The two cases with osseointegration to a previous implant were faster to osteointegrate following revision (both six months) than those without previous extracortical bone growth or osseointegration (mean 12.3 months (8 to 15); p = 0.068).

Discussion
This study is the first to report osseointegration of HA-coated collars on massive endoprostheses used in revision surgery. Previous studies have shown their use in primary cases may help reduce the incidence of aseptic loosening.3

This work has shown that the benefits of this adjunct in revision endoprostheses and consequent outcomes are more complicated than first thought. The frequency of osseointegration to ≥ 1 collar side in this group of patients undergoing revision surgery was lower (43.6%,
Table II. Summary of results and differences seen in osseointegration to at least one side of the collar and time to osseointegration first seen in subgroup analyses.

| Clinical factors                  | N  | Osseointegration to ≥ 1 side, % | Odds ratio (95% CI) | p-value | Mean time to osteointegrate, months (range) | p-value |
|-----------------------------------|----|---------------------------------|----------------------|---------|-----------------------------------------------|---------|
| **Sex**                           |    |                                 |                      |         |                                               |         |
| Male                              | 16 | 50.0                            | 1.56 (0.42 to 5.65)  | 0.502   | 12.0 (5 to 21)                                | 0.686   |
| Female                            | 23 | 39.1                            | N/A                  | N/A     | 13.9 (5 to 45)                                | N/A     |
| **Age, yrs (continuous)**         |    |                                 |                      |         |                                               |         |
| > 39                              | 20 | 55.0                            | 2.54 (0.72 to 9.80)  | 0.145   | 14.6 (6 to 45)                                | 0.311   |
| ≥ 40                              | 19 | 31.6                            | N/A                  | N/A     | 10.2 (5 to 21)                                | N/A     |
| **Smoker**                        |    |                                 |                      |         |                                               |         |
| Yes                               | 4  | 50.0                            | 1.42 (0.17 to 11.4)  | 0.736   | 12.0 (9 to 15)                                | 0.439   |
| No                                | 34 | 41.2                            | N/A                  | N/A     | 12.6 (5 to 45)                                | N/A     |
| **Primary procedure**             |    |                                 |                      |         |                                               |         |
| Revision arthroplasty             | 7  | 14.3                            | N/A                  | N/A     | 5 (N/A)                                       | 0.987   |
| Oncological                       | 32 | 50.0                            | 6.82 (0.65 to 55.66) | 0.115   | 13.5 (5 to 45)                                |         |
| **Indication for revision**       |    |                                 |                      |         |                                               |         |
| Aseptic loosening                 | 15 | 26.7                            | N/A                  | N/A     | 11.3 (5 to 21)                                | N/A     |
| Infection                         | 12 | 58.3                            | 3.8 (0.76 to 19.47)  | 0.103   | 15.6 (6 to 45)                                | 0.511   |
| Implant failure                   | 7  | 42.9                            | 2.1 (0.31 to 13.57)  | 0.451   | 11.7 (6 to 15)                                | 0.580   |
| Periprosthetic fracture           | 5  | 60.0                            | 4.1 (0.49 to 34.50)  | 0.191   | 10.7 (5 to 21)                                | 0.620   |
| **Implant**                       |    |                                 |                      |         |                                               |         |
| Proximal femoral                  | 10 | 40.0                            | N/A                  | N/A     | 9.8 (5 to 21)                                 | N/A     |
| Distal femoral                    | 24 | 45.8                            | 1.3 (0.28 to 5.68)   | 0.755   | 14.7 (6 to 45)                                | 0.125   |
| Proximal tibial                   | 4  | 25.0                            | 0.5 (0.04 to 6.68)   | 0.600   | 14 (N/A)                                      | 0.196   |
| Tibial diaphyseal                 | 1  | 100.0                           | N/A                  | N/A     | 6 (N/A)                                       | 0.927   |
| **Number of previous revision operations** |    |                                 |                      |         |                                               |         |
| 0                                 | 17 | 41.2                            | N/A                  | N/A     | 18.1 (5 to 45)                                | N/A     |
| 1                                 | 7  | 42.9                            | 1.07 (0.18 to 6.36)  | 0.939   | 8.3 (6 to 12)                                 | 0.082   |
| 2                                 | 5  | 80.0                            | 5.7 (0.52 to 62.66)  | 0.154   | 9.5 (5 to 14)                                 | 0.085   |
| 3                                 | 4  | 50.0                            | 1.43 (0.16 to 12.70) | 0.749   | 11.5 (9 to 14)                                | 0.401   |
| 4                                 | 5  | 20.0                            | 0.35 (0.03 to 3.92)  | 0.399   | 8 (N/A)                                       | 0.232   |
| 5                                 | 1  | 0.0                             | N/A                  | N/A     | N/A                                           | N/A     |
| **Previous osseointegration seen**|    |                                 |                      |         |                                               |         |
| Yes                               | 3  | 66.7                            | 5.33 (0.54 to 13.08) | 0.232   | 6 (N/A)                                       | 0.068   |
| Overgrowth Only                   | 20 | 50.0                            | 2.66 (0.34 to 82.83) | 0.227   | 14.6 (5 to 45)                                | 0.588   |
| No                                | 11 | 27.3                            | N/A                  | N/A     | 12.3 (8 to 15)                                | N/A     |
| **Confirmed previous infection**  |    |                                 |                      |         |                                               |         |
| Yes                               | 18 | 50.0                            | 1.65 (0.45 to 5.82)  | 0.456   | 15.0 (5 to 45)                                | 0.548   |
| No                                | 21 | 38.1                            | N/A                  | N/A     | 10.8 (5 to 21)                                | 0.990   |
| **Arthroplasty with previous infection** |    |                                 |                      |         |                                               |         |
| Oncological                       | 11 | 72.7                            | N/A                  | N/A     | 16.3 (6 to 45)                                | N/A     |
| **Oncological with no evidence of previous infection** |    |                                 |                      |         |                                               |         |
| Adjuvant/neo-adjuvant therapies†  |    |                                 |                      |         |                                               |         |
| Chemotherapy                      | 13 | 61.5%                           | 1.60 (0.30 to 8.49)  | 0.581   | 11 (6 to 21)                                  | 0.833   |
| Radiotherapy                      | 2  | 0.0%                            | 1 (N/A)              | N/A     | N/A                                           | N/A     |
| Chemotherapy plus radiotherapy    | 2  | 50.0%                           | 1.00 (0.05 to 20.83) | 1.000   | 14 (N/A)                                      | 0.650   |
| None                              | 10 | 50.0%                           | N/A                  | N/A     | 16.8 (5 to 45)                                | N/A     |

P-values for differences in osseointegration were calculated using univariate logistic regression. P-values for differences in time to osseointegration first seen were calculated using ordinal logistic regression.

*Five procedures were the first hydroxyapatite-collar coated implant that the patient had received.
†Arthroplasty cases not included; five cases had no clear documentation so excluded from analysis.
N/A, not applicable.
17/39) than reported rates following primary endoprosthetic implantation (65% to 81%).

No specific individual clinical factors were predictive of osseointegration across the whole cohort (Table II). However, when aseptic loosening was the indication for revision, patients aged > 39 years were less likely to show osseointegration. This may be because older patients underwent primary surgery for non-oncological reasons and the failure of the primary and subsequent prosthesis may have been multifactorial.

Outcomes of primary DFAs and PTAs are worst with respect to aseptic loosening with reported rates of up to 35% and 46% respectively. Consistent with the literature, the most common indication for revision endoprosthesis in this study was aseptic loosening (38.5%, 15/39). However, these patients were less likely to show osseointegration (26.7%, 4/15) compared to the other indications for revision.

Patients aged > 39 years without osseointegration were more likely to show grade 2 rather than grade 1 bone growth pattern, suggesting that despite growth, this bone fails to integrate with the HA-coated collar. Interestingly, in other implant designs used in humans where porous rather than HA-coated collars are used, despite evidence of extra-cortical bone development, ongrowth to the implant was not shown (grade 2 appearance).

The oncological group appeared to have benefitted the most from the HA-collar design with 50.0% (16/32) showing osseointegration to ≥ 1 side compared to 14.3% (1/7) in the failed arthroplasty cohort (p = 0.115). This was particularly pronounced when reviewing current or previous infection status. This analysis was performed to assess whether history or treatment of a local infection caused longstanding changes in the biological environment that would affect osseointegration. Patients who had primary surgery for an oncological indication with current or previous infection were significantly more likely to show osseointegration on ≥ 1 collar side than the arthroplasty group, of whom all cases had current or previous infection. Care has to be taken in extrapolating findings as the failed arthroplasty group was significantly older (mean 70.7 vs 36.5 years; p < 0.001) and underwent more previous revision surgeries (mean 3.14 vs 1.00; p < 0.001) than the oncological cases with previous or current infection. Although these two factors individually did not show significant differences in presence of osseointegration, these findings suggest HA-coated collars showed limited benefit for non-oncological patients undergoing revision for failed arthroplasty with current or previous infection.

Within the oncological group, cases with current or previous infection were more likely to show osseointegration to ≥ 1 collar side than those without history of infection (OR 4.3; p = 0.071). Of the 11 oncological cases with current or previous infection, ten underwent revision for current infection, the other for aseptic loosening following previous infection. This suggests that in spite of infection new bone growth appears more likely to occur. The reason for the difference between these groups is not fully understood and could not be accurately reviewed in this retrospective study but is an interesting avenue for future work. It could be postulated that, the HA-coated collar design may have better results in the oncology cases with history of infection due to more aggressive bone and tissue debridement at revision surgery. As this is not repeated for similar cases in the arthroplasty group, it may represent the reduced potential for osseointegration in the older population, despite attempts to improve the biological environment with aggressive debridement during revision for infected arthroplasty (Figure 4b).

Chemotherapy has been associated with reduced bone formation in the first year following endoprosthesis implantation. However, this study showed no significant difference in osseointegration, including when adjusted for history of infection.

Using the ongrowth grading system, it was noted that bone formed adjacent to the HA-coated collar but did not integrate with the implant surface (grade 2) in 41.0% (16/39) of cases (Figure 2). Sankar et al reported that over a five-year follow-up of primary implants, 7/7 (100%) with this pattern of growth required revision. Interestingly, in our cohort, one patient with a grade 2
pattern had an implant in situ for greater than five years without revision.

This study is the first to report time to osseointegration to HA-coated endoprosthetic collars at a mean of 13 months. The shorter time to osseointegration in PFAs (9.8 months) may relate to differences in biomechanical forces applied to the implant. Overall, four patients in this cohort had follow-up of less than 13 months (mean time to first osseointegration), two of which showed osseointegration (at eight and nine months). The other two patients had their latest follow-up recorded in this study at 12 months. It is possible that these two patients may subsequently show osseointegration. It has been shown, in only one previous study, that by two years osseointegration to primary implants may be complete. Due to its retrospective nature, this study was limited by radiographs not being performed at specific time points. This meant that pinpointing the specific time at which osseointegration starts and its progression over time could not definitively be defined. Given that osseointegration can be seen as early as five months following endoprosthesis implantation, further prospective work with radiographs at pre-determined time points should be performed to assess how osseointegration progresses with time.

Longer follow-up of this cohort and future cases will allow improved analyses of osseointegration grades in revision endoprostheses and better understanding of the effect of clinical factors. Additionally, this study only assessed bone growth following latest revision. Analyses of osseointegration at prior failure may provide useful information.

Although this study was performed at a high-volume orthopaedic tertiary referral centre, the cohort sizes were small, representing the specialist case nature with low statistical power. It is not possible to conclude about individual outcome predictors due to wide clinical variations in subgroup analyses.

This study analyzed consistent practice of bone resection without attempt to preserve a periosteal sleeve to reattach to the HA-collar. In cases involving oncological and infection issues, periosteal preservation can be a concern. Further analysis would be required to determine if such practice alters outcomes of osseointegration. In this study, the collar size was matched to the bone diameter at the time of resection. To determine if collar size/mismatch influences osseointegration, studies design to prospectively analyze this issue would be beneficial.

The analysis used in this study was for radiological osseointegration. Fibrous ongrowth of the collar, which can improve stability and microscopic extra-cortical bone bridging could be assessed using histological retrieval studies.

Further studies including use of autogenous bone-grafting, porous collars, and stem cell augmentation in human studies and osteogenic protein-1 in animal models have shown varying results but combining small pores (700 μm) with internal and external HA-coated collars has shown up to five-times increased bone integration compared to solid grooved designs.

This study highlights poor osseointegration of HA-coated collars in massive endoprostheses following revision surgery, independent of indication. Osseointegration to HA-coated collars was limited and had lower rates (43.6%, 17/39) than reported following primary surgery, suggesting their benefit may be more limited than expected when used in revision surgery.

Age appears important in influencing outcome. Young patients, aged < 40 years, who undergo revision surgery following initial oncological surgery may benefit most from this collar design. Additionally, there also appears to be benefit from their use in revision oncological cases with a history of current or previous infection.

Revision surgery for aseptic loosening was associated with the poorest results, with 73.3% (11/15) of cases showing no osseointegration. HA-coated collars showed limited benefit for non-oncological patients undergoing revision for failed arthroplasty with current or previous infection. Further developments of collar design and understanding of clinical factors and biological environment may help define optimum conditions for bone integration and implant survival.

**Take home message**

- This study highlights poor osseointegration of HA-coated collars in massive endoprostheses following revision surgery, independent of indication.
- Age appears to be the most important clinical factor with young patients undergoing revision surgery following initial oncological surgery may benefit most from this collar design.

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Funding statement:
- Although none of the authors has received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article, benefits have been or will be received but will be directed solely to a research fund, foundation, educational institution, or other non-profit organization with which one or more of the authors are associated.

ICMJE COI statement:
- B. Davies, B. Davies, and C. Gerrand report consultancy and departmental grants/ grants pending from Stryker, which are unrelated to this article. A. Johnston declares fees for participation in review activities, such as data monitoring boards, statistical analysis, endpoint committees, from Stryker, which occurred after this article was undertaken, and consultancy and travel/accommodations/meeting expenses from Adler, payment for lectures from Surgical Innovations, and being Editor of OUP, all of which are unrelated.

Open access funding:
- Funded by Royal National Orthopaedic Hospital, Stanmore, UK.

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