



# Synthetic porous ceramic compared with autograft in scoliosis surgery

A PROSPECTIVE, RANDOMISED STUDY OF 341 PATIENTS

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**W**e have evaluated the use of a synthetic porous ceramic (Triosite) as a substitute for bone graft in posterior spinal fusion for idiopathic scoliosis. In a prospective, randomised study 341 patients at five hospitals in the UK and France were randomly allocated either to autograft from the iliac crest or rib segments (171) or to receive Triosite blocks (170). All patients were assessed after operation and at 3, 6, 12 and 18 months.

The two groups were similar with regard to all demographic and baseline variables, but the 184 treated in France (54%) had Cotrel-Dubouset instrumentation and the 157 treated in the UK usually had Harrington-Luque implants. In the Triosite group the average Cobb angle of the upper curve was 56°, corrected to 24° (57%). At 18 months, the average was 26° (3% loss). In the autograft group the average preoperative upper curve of 53° was corrected to 21° (60%). At 18 months the mean curve was 25° (8% loss). Pain levels after operation were similar in the two groups, being mild in most cases. In the Triosite

group only three patients had problems of wound healing, but in the autograft group, 14 patients had delayed healing, infection or haematoma in the spinal wound. In addition, 15 autograft patients had pain at the donor site at three months. Seven had infections, two had haematoma and four had delayed healing.

The haematological and serum biochemistry results showed no abnormal trends and no significant differences between the groups. There were no adverse events related to the graft material and no evidence of allergenicity.

Our results suggest that Triosite synthetic porous ceramic is a safe and effective substitute for autograft in these patients. Histological findings on biopsy indicate that Triosite provides a favourable scaffolding for the formation of new bone and is gradually incorporated into the fusion mass.

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The use of bone grafting in surgery for scoliosis is well established.<sup>1</sup> Autograft has traditionally been considered to be an ideal material, but obtaining it causes problems such as increased blood loss and operating time,<sup>2</sup> pain at the donor site, and inadequate amounts in young patients and those with neuromuscular scoliosis.<sup>3,4</sup> Banked allograft bone is sometimes available, but it is inferior to autogenous bone and has known risks of bacterial contamination and viral transmission.<sup>5</sup>

We have investigated the clinical performance of a synthetic porous ceramic (Triosite; Zimmer Ltd, Swindon, UK). Calcium phosphate ceramics are known to be safe and non-allergenic with good bone-bonding capacity. They have been used as substitutes for bone graft in orthopaedic, maxillofacial and dental operations.<sup>6</sup> Triosite is a biphasic calcium phosphate ceramic containing hydroxyapatite (60%) and betatricalcium phosphate (40%) in macroporous form. It is commercially available as blocks and granules. Its porous structure has been shown to provide a favourable scaffolding for bone growth.<sup>7</sup>

Our multicentre study evaluated the use of Triosite in patients having posterior spinal fusion for idiopathic scoliosis.

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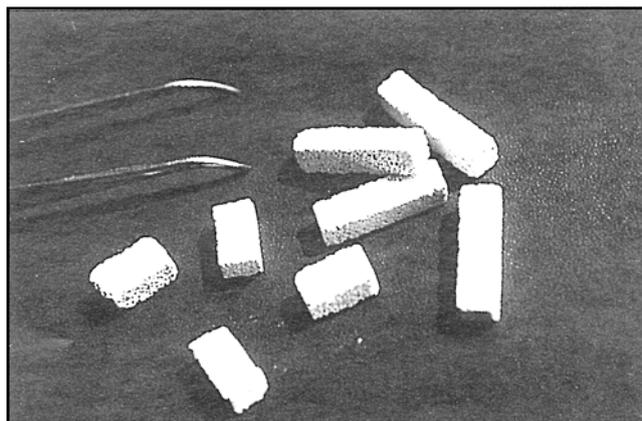


Fig. 1

Triosite blocks of 1 and 2 cm in size (see text).

## Patients and Methods

Our prospective, randomised trial compared autograft with Triosite in 341 patients with idiopathic scoliosis, between the ages of 11 and 25 years. These patients entered the trial at five hospitals in the UK and France, for operations between November 1989 and October 1992. Ethical approval was obtained at each hospital before the study, and all patients and/or their parents gave their informed consent.

Of the 341 patients in the study, 170 had Triosite and 171 had autograft. The groups were similar with regard to median age (Triosite 16.2 years (11.7 to 24.9); autograft 15.9 years (11.4 to 25.6), gender ratio (Triosite 146 F:24 M; autograft 135 F:35 M, 1 not specified) and for all other demographic variables. There were no statistical differences between the baseline variables for patients from different countries.

For posterior spinal fusion we used either the Cotrel-Dubousset system (184 (54%) French patients) or Harrington-Luque instrumentation (155 (46%) UK patients), with two UK patients having Moduloc Mark 1 implants. In France, the standard technique described by Cotrel and Dubousset involved distraction and derotation.<sup>8</sup> The Harrington-Luque procedure used standard Harrington rods with sublaminar wires at most segments. At all centres the surgical technique was a classic posterior spinal fusion with decortication and excision of the facet joints. In the UK, 74 patients had anterior release as a separate operation before the posterior fusion and anterior corrective instrumentation (Zielke or Webb-Morley) was used in many of these patients to correct the lumbar or thoracolumbar curve. Costoplasty was sometimes performed as a simultaneous procedure at the time of surgery for posterior scoliosis; in these cases the rib segments were used for autografts.<sup>9</sup>

Randomisation into two groups was by a predetermined

schedule which was stratified for each surgeon. The method was by opening a sealed envelope bearing the patient number immediately before operation.

In most of the patients receiving autograft, iliac bone was taken through a unilateral approach to the posterior ilium by a separate skin incision. The iliac crest and its growth plate were preserved, cortical and cancellous bone chips being obtained from the area below this. The autograft was supplemented by bone chips obtained locally from the spine.

The ceramic graft substitute was provided as sterile biphasic calcium phosphate blocks (Triosite, Zimmer) either  $5 \times 5 \times 10$  mm or  $5 \times 5 \times 20$  mm containing 60% hydroxyapatite and 40% betatricalcium phosphate with 50% porosity and macropores from 400 to 600  $\mu$ m in diameter (Fig. 1). At operation, blocks of Triosite were placed on the open facets and at the base of decorticated transverse processes, using an average of three blocks for each vertebral segment. The Triosite blocks were supplemented by and covered with free bone chips obtained locally from the spine. Attention was paid to close contact between the Triosite blocks and the decorticated vertebrae to allow osteogenic elements to infiltrate the Triosite and to maximise fusion.

All patients received perioperative cephalosporin which was usually continued postoperatively by intravenous injection. The wounds were sutured in three layers, and usually one suction drain was used on each side of the spine.

Postoperatively, the UK patients wore a removable front-opening subortholene brace for six months and were asked to refrain from contact sports for one year. The French patients had no external splintage.

Postoperative assessments were made at 5 to 10 days and at 3, 6, 12 and 18 months. We recorded the duration of the operations and the transfusion requirements. Pain and wound healing were assessed at the donor sites and at the spine. Routine haematological and serum biochemistry tests were performed preoperatively and at three months, for haemoglobin, WBC count, sodium, potassium, bilirubin, aspartate transferase, alanine transferase, alkaline phosphatase, albumin, calcium and phosphate.

Anteroposterior and lateral standing radiographs were taken preoperatively, at 5 to 10 days after operation and at 6, 12 and 18 months. We recorded Risser grades and Cobb angles.<sup>10</sup> Six different biopsies of Triosite graft material were obtained from patients who required reoperation for hook malplacement, pseudarthrosis, residual costoplasty or removal of prominent metal implant.

**Statistical analysis.** All continuous variables suspected to be normally distributed were tested for evidence of non-normality by plotting the Studentised residuals and by use of the PROC UNIVARIATE procedure in SAS, which derives the Shapiro-Wilk statistic (W). If this was  $<0.05$  we assumed a non-normal distribution and used non-parametric methods, such as the Wilcoxon rank-sum test (PROC NPAR1WAY in SAS). If the W statistic was  $>0.05$ ,

we used parametric testing by analysis of variance (PROC ANOVA and PROC GLM in SAS). Confidence intervals are given at the 95% level. Binary and nominal data were analysed by chi-squared or Fisher's exact tests (PROC FREQ in SAS).

## Results

**Operative details.** The distribution of Risser signs was similar for both groups, being 4 or 5 in 57% of the Triosite patients and 66% of the autograft patients. At least 11 vertebrae were fused in 69% of the Triosite group and in 63% of the autograft group. For the Triosite group, a mean total of 17.2 cm and 16.1 cm blocks was used and a mean volume of 36 cm<sup>3</sup> of local bone chips. The volume of autograft bone from donor sites was measured in standard laboratory measuring cylinders in 59% of autograft patients. The mean volume was 55 cm<sup>3</sup>, supplemented by a mean volume of 30 cm<sup>3</sup> of local spinal bone.

The different instrumentation and operative techniques produced a significantly longer mean operating time for French patients ( $p < 0.001$ ). The 95% confidence intervals for between-treatment differences in duration of surgery were -6.944 to +19.484, and therefore treatment differences were analysed for individual countries. In the UK, the mean duration of operation was 156 minutes for the Triosite group and 154 minutes for the autograft group. In France, the mean operating time was 211 minutes for the Triosite group and 225 minutes for the autograft group.

A number of patients in the autogenous group, mainly in the UK, did not require a separate incision at the donor site as rib bone had been harvested during a previous costoplasty. When these patients were excluded from an analysis of operating time, the differences consistently favoured the Triosite group. An analysis of variance using treatment group and instrumentation showed that operations with Triosite were significantly shorter ( $p = 0.036$ ) as were the Harrington-Luque procedures ( $p < 0.001$ ). The effect of the choice of instrumentation on operating time in the two treatment groups was not significant ( $p = 0.866$ ).

There was a mean transfusion volume of 1214 ml in the triosite group and 1229 ml in the autograft group ( $p = 0.58$ ). For UK patients it was 1500 ml which was significantly higher than the 1000 ml for French patients ( $p < 0.001$ ). In France almost all the transfusions were of autologous blood donated before operation, collected peri-operatively or both. All transfused blood in the UK was obtained from blood banks.

We have complete data for the 18-month follow-up in 89% of the 341 patients. Twelve patients in the autograft group and ten in the Triosite group were lost to follow-up before this time for reasons unrelated to the surgery, such as relocation. Two other autograft patients were found not to comply with the entry criteria and were withdrawn. Consent was withheld by one patient. Four autograft and two

Triosite patients were withdrawn because of the need for reoperation. In the autograft group one reoperation was needed after a road-traffic accident and a further five for problems with the instrumentation. One other patient in the Triosite group was excluded because of the deterioration of a previously undiagnosed osteosarcoma of the spine distal to the instrumented region. All available data on the patients who were withdrawn were included in the intention-to-treat analysis.

**Radiography.** Table I gives details of the measurements of the Cobb angle. The mean preoperative angle of the upper curve was 53° in the Triosite group and 56° in the autograft group. At 18 months correction of the upper curve was 53% for the Triosite group and 54% for the autograft group. The mean loss of correction of this curve between the second postoperative week and 18 months was 8% for the Triosite group and 4% for the autograft group. The confidence interval for this between-treatment difference was from -1.1953 to +2.0703. During the same period, correction of the lower curve was 57% for the Triosite group and 56% for the autograft group and loss of correction over the 18-month follow-up was 7% and 4%, respectively. The confidence interval for this between-treatment difference was from -1.5 to +2.3.

Statistical analysis of these variables showed no significant differences. The loss of correction of the upper curve by 18 months, however, in the patients receiving Harrington instrumentation (Triosite 7%, autograft 9%) was significantly greater than for those receiving Cotrel-Dubousset instrumentation (Triosite 2%, autograft 4%;  $p < 0.001$ ). The difference in mean loss of correction between the two methods of instrumentation was not statistically significant for the lower curve ( $p = 0.107$ ).

**Spinal pain.** Sixty patients in the series complained of pain in the operated region, usually mild in nature. Before operation, 31 Triosite patients and 29 with autograft had spinal pain; at 18 months these numbers had fallen to 24 and 18, respectively. There was no statistically significant difference between the two groups ( $p = 0.298$ ).

**Healing of the spinal wound.** During the 18 months of follow-up there were 14 recorded problems with healing of the spinal wound in the autograft group (delayed healing, infection or haematoma) and three in the Triosite group. Three patients in each group required treatment with antibiotics; surgical repair was required in another three patients in the autogenous group.

**Problems at the donor site.** At three months, 15 (9%) of the autograft patients who were assessed reported mild pain at the donor site and at 18 months there were ten (6%) (Table II).

Seven patients had infection at the donor site, either early or late. A haematoma was seen in two patients and delayed healing, for up to three months, in four.

**Haematology and serum biochemistry.** We assessed the results of the haematological and serum biochemistry investigations before operation and after three months,

**Table I.** Radiological results showing mean Cobb angles and (ranges) with *percentage* corrections

|                 | Upper curve           |                       | Lower curve*          |                        |
|-----------------|-----------------------|-----------------------|-----------------------|------------------------|
|                 | Triosite              | Autograft             | Triosite              | Autograft              |
| All patients    | n = 168               | n = 159               | n = 119               | n = 112                |
| Preoperative    | 53 (6 to 118)         | 56 (4 to 106)         | 46 (12 to 85)         | 48 (7 to 141)          |
| Postoperative   | 21 (0 to 62)<br>(60%) | 24 (0 to 90)<br>(57%) | 17 (0 to 58)<br>(63%) | 19 (0 to 106)<br>(60%) |
| 18 months       | 25 (0 to 62)<br>(53%) | 26 (1 to 60)<br>(54%) | 20 (0 to 63)<br>(57%) | 21 (0 to 50)<br>(56%)  |
| Correction loss | 8%                    | 4%                    | 7%                    | 4%                     |
| French series   | n = 90                | n = 87                | n = 71                | n = 64                 |
| Preoperative    | 49 (19 to 84)         | 52 (10 to 95)         | 45 (143 to 70)        | 48 (7 to 141)          |
| Postoperative   | 17 (0 to 44)<br>(65%) | 20 (2 to 60)<br>(62%) | 14 (0 to 35)<br>(69%) | 17 (0 to 36)<br>(64%)  |
| 18 months       | 19 (0 to 46)<br>(61%) | 21 (2 to 40)<br>(60%) | 16 (0 to 35)<br>(64%) | 18 (0 to 40)<br>(62%)  |
| Correction loss | 4%                    | 2%                    | 4%                    | 2%                     |
| UK series       | n = 78                | n = 72                | n = 48                | n = 48                 |
| Preoperative    | 57 (6 to 118)         | 60 (4 to 106)         | 49 (12 to 85)         | 52 (20 to 141)         |
| Postoperative   | 27 (6 to 62)<br>(53%) | 28 (0 to 90)<br>(53%) | 20 (0 to 58)<br>(59%) | 22 (1 to 106)<br>(58%) |
| 18 months       | 32 (5 to 62)<br>(44%) | 32 (1 to 60)<br>(47%) | 25 (5 to 63)<br>(49%) | 25 (6 to 50)<br>(52%)  |
| Correction loss | 9%                    | 7%                    | 10%                   | 6%                     |

\* some patients had only one curve hence there are fewer "lower curves"

**Table II.** Number (*percentage*) of autogenous graft patients reporting pain at the donor site

| Stage (mth) | Number |
|-------------|--------|
| 3           | 15 (9) |
| 6           | 15 (9) |
| 12          | 6 (4)  |
| 18          | 10 (6) |

recording the numbers of patients with values outside the normal laboratory ranges at the two assessments. We found no abnormal trends and no apparent differences between the two groups.

**Adverse events.** Adverse events were recorded for 12% of patients, 22 from the autograft group and 20 from the Triosite group, but none was directly related to the grafting material. Hook movement occurred in six autograft and eight Triosite patients and other instrument-related problems such as broken wires or loosening were seen in four autograft patients and two with Triosite.

There were minor neurological problems in four patients with autografts and one with Triosite, and postoperative respiratory problems occurred in one Triosite and three autograft patients.

**Histological examination.** Biopsy specimens were obtained from six Triosite patients who had reoperations for problems with the implants such as the refixation of hooks. The specimens showed osteoconduction inside the ceramic pores and confirmed the very gradual resorption of Triosite into new bone, with some ingrowth as early as two weeks (Fig. 2).

At three years after surgery, one specimen showed a

piece of Triosite engulfed in fibrous tissue and therefore not incorporated into the fusion mass (Fig. 3). Another area in the same patient showed true osseous incorporation of the Triosite (Fig. 4). It seems that the Triosite should be sandwiched between decorticated laminae and locally available autogenous bone to protect it from invasion by fibrous tissue. Smaller pieces of Triosite would probably have been converted to bone more quickly.

## Discussion

Our results suggest that Triosite provides an attractive alternative to autogenous grafting for scoliosis surgery. An important advantage is the absence of a donor site and its problems. We saw no complications from the implantation of a foreign material.

In our autogenous group the incidence of reported pain at the iliac donor site was similar to that reported by Summers and Eisenstein<sup>11</sup> who commented that a feature of such pain is its resistance to treatment. Not all of our autograft patients required iliac-crest bone. We used rib bone harvested during costoplasty in some, but those who had a separate donor-site incision had a longer duration of operation.

Our radiological results for correction of deformities are comparable to those reported elsewhere,<sup>12</sup> and reconfirm that both the Cotrel-Dubousset and Harrington-Luque methods allow satisfactory correction and stabilisation of scoliosis. The small loss of correction over 18 months was also consistent with other results. Our large numbers were designed to overcome interobserver differences in radio-



Fig. 2

Medium-power photomicrograph of a section of Triosite removed eight days after implantation, showing red blood cells and occasional fibroblasts within the pores (×46).

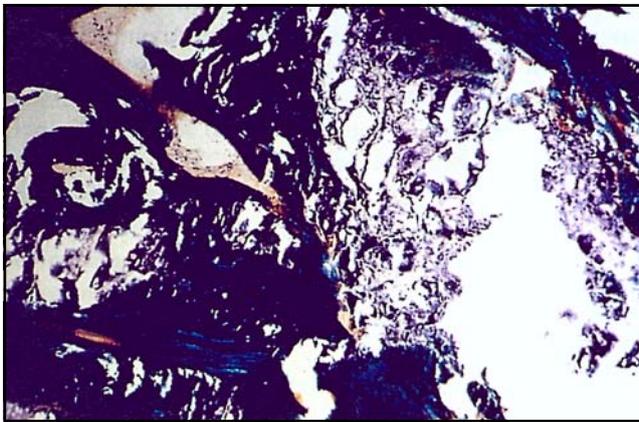


Fig. 3

High-power photomicrograph of an undecalcified section of a fusion mass biopsy obtained at three years. The Triosite is at the top and is surrounded by fibrous tissue which has prevented incorporation into the fusion mass below. Triosite is engulfed in fibrous tissue unless it is adjacent to bone (Goldner's stain ×205).



Fig. 4

Photomicrograph of an undecalcified section showing residual Triosite three years after scoliosis surgery (greyish purple) incorporated within mineralised lamellar bone (green) with some active osteoid seams (orange) (Goldner's stain ×205).

logical assessment, since variation in excess of 5° of the Cobb angle has been reported by some authors.<sup>13</sup>

The Triosite ceramic which we used is a mixture of hydroxyapatite and betatricalcium phosphate. The latter dissolves rapidly in vivo and new bone is formed to replace it.<sup>7</sup> Hydroxyapatite has a low solubility, remains stable for a longer period and undergoes chemical bonding by the formation of a thin layer of apatite.<sup>7</sup> The presumed advantage of the mixture of these two different materials in optimal proportions is considered to be the controlled rate of release of calcium and phosphate combined with long-term stability and orderly bone growth. It has recently been shown that the compressive strength of Triosite increased significantly within three weeks of implantation into rabbit bone, presumably due to both the chemical transformation of the ceramic and conductive bone ingrowth.<sup>14</sup>

There is no evidence to suggest that Triosite provides any stimulus to bone formation over that provided by the architecture of the implant. Near bleeding bone, there seems to be an adequate stimulus for the formation of new bone, provided that appropriate scaffolding is available for vascular invasion and osteoblast proliferation. Our histological findings provide evidence of gradual incorporation into the fusion mass, provided that the material is not adjacent to muscle. This situation may lead to encapsulation by fibrous tissue and exclusion from the fusion mass.

**Conclusions.** Our study has shown that Triosite blocks are a useful addition to and substitute for autogenous grafts in spinal fusion for the correction of idiopathic scoliosis. We have confirmed the safety and absence of allergenicity of Triosite and our histological results warrant further research with alternative formulations of Triosite such as granules which may be more rapidly incorporated into bone.

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