**A novel osseointegrated percutaneous prosthetic system for the treatment of patients with transfemoral amputation: A prospective study of 51 patients.**



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■ TRAUMA

# A novel osseointegrated percutaneous prosthetic system for the treatment of patients with transfemoral amputation

## A PROSPECTIVE STUDY OF 51 PATIENTS

R. Brånemark,
Ö. Berlin,
K. Hagberg,
P. Bergh,
B. Gunterberg,
B. Rydevik

*From Department of Orthopaedics, Institute of Clinical Sciences, University of Gothenburg Sahlgrenska University Hospital. Gothenburg, Sweden*

**Patients with transfemoral amputation (TFA) often experience problems related to the use of socket-suspended prostheses. The clinical development of osseointegrated percutaneous prostheses for patients with a TFA started in 1990, based on the long-term successful results of osseointegrated dental implants.**

**Between1999 and 2007, 51 patients with 55 TFAs were consecutively enrolled in a prospective, single-centre non-randomised study and followed for two years. The indication for amputation was trauma in 33 patients (65%) and tumour in 12 (24%). A two-stage surgical procedure was used to introduce a percutaneous implant to which an external amputation prosthesis was attached. The assessment of outcome included the use of two self-report questionnaires, the Questionnaire for Persons with a Transfemoral Amputation (Q-TFA) and the Short-Form (SF)-36.**

**The cumulative survival at two years' follow-up was 92%. The Q-TFA showed improved prosthetic use, mobility, global situation and fewer problems (all $p < 0.001$). The physical function SF-36 scores were also improved ($p < 0.001$). Superficial infection was the most frequent complication, occurring 41 times in 28 patients (rate of infection 54.9%). Most were treated effectively with oral antibiotics. The implant was removed in four patients because of loosening (three aseptic, one infection).**

**Osseointegrated percutaneous implants constitute a novel form of treatment for patients with TFA. The high cumulative survival rate at two years (92%) combined with enhanced prosthetic use and mobility, fewer problems and improved quality of life, supports the 'revolutionary change' that patients with TFA have reported following treatment with osseointegrated percutaneous prostheses.**

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■ R. Brånemark, MD, PhD, Orthopaedic Surgeon, Associate Professor
■ Ö. Berlin, MD, PhD, Orthopaedic Surgeon, Associate Professor
■ K. Hagberg, RPT, PhD, Physiotherapist, Associate Professor
■ P. Bergh, MD, PhD, Orthopaedic Surgeon
■ B. Gunterberg, MD, PhD, Orthopaedic Surgeon, Associate Professor
■ B. Rydevik, MD, PhD, Orthopaedic Surgeon, Professor
Sahlgrenska University Hospital, Department of Orthopaedics, Institute of Clinical Sciences, University of Gothenburg, Gothenburg, Sweden.

Correspondence should be sent to Dr R. Brånemark; e-mail: rickard.branemark@orthop.gu.se


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Patients with transfemoral amputation (TFA) frequently experience problems related to the use of socket-suspended prostheses,[1-3] and these problems increase with short or deformed stumps.[4] Based on long-term results using osseointegrated titanium implants in other specialties,[5-8] we have developed an osseointegrated prosthesis for TFA. In this paper we report the results of a two-year follow-up of 51 consecutive patients.

## Patients and Methods

This was a prospective, single-centre, non-randomised study in accordance with the European standard for clinical investigations of medical devices (EN-540) and for which ethical approval had been obtained. Pre- and post-operative data regarding the osseointegrated prostheses were compared for each patient. A total of 51 patients with TFA were included in the study between 1999 and 2007, and each patient was followed for two years. All operations were performed at Sahlgrenska University Hospital, Gothenburg, Sweden and removal of the implant was the end-point for failure.

A total of 45 patients had a unilateral and six a bilateral TFA (Table I). The total number of limbs evaluated was 55, as four of 51 patients had bilateral TFAs and were treated bilaterally and two with bilateral TFAs were treated on one side only. The main reasons for amputation were trauma and malignant tumour. On entry to the study, most patients were using conventional socket-suspended prostheses (42/51), but nine did not use a prosthesis. Of these, eight had been unable to obtain a comfortable prosthesis and one had not tried using a prosthesis due to the extreme shortness of the amputation stump.

The inclusion and exclusion criteria are summarised in Table II and the design of the study and patient participation in Figure 1.

**Treatment protocol.** The implant (OPRA Implant System (Osseointegrated Prostheses

**Table I.** Demographics

| Variable | |
|---|---|
| Patients (n) | 51 |
| Male gender (n, %) | 28 (*55*) |
| | |
| At amputation | |
| Mean patient age (yrs) (range) [median; SD] (n = 50 patients)† | 32 (13 to 64) [32; 14] |
| Amputation (n, %)* | |
| Unilateral | 45 (*88*) |
| Bilateral | 6 (*12*) |
| Reason for amputation (n, %) | |
| Trauma | 33 (*65*) |
| Tumour | 12 (*24*) |
| Other | 6 (*12*) |
| | |
| At inclusion | |
| Mean patient age (yrs) (range) [median; SD] | 44 (20 to 65) [46; 12] |
| Time from amputation to surgery S1 (yrs) (range) [median; SD] | 12 (1 to 42) [8; 11] |
| Concomitant injuries/defects (n) | |
| Contralateral transtibial amputation | 1 |
| Other defect on contralateral leg | 4 |
| Paralytic arm | 2 |
| Mean estimated weight (kg) (range) [median; SD] (n = 50 patients)‡ | 84 (50 to 129) [83; 19] |
| Smoker (n, %) | 11 (*22*) |
| Prosthesis-user (≥ 1 day/week) | 42 (*82*) |
| Country of residence (n, %) | |
| United Kingdom | 1 (*2*) |
| Norway | 14 (*27*) |
| Spain | 11 (*22*) |
| Sweden | 25 (*49*) |
| Extremities treated (n) | 55 (4 bilateral patients) |
| Mean length of femur at inclusion (cm) (range) [median; SD] (n = 55 limbs)§ | 22.4 (13.1 to 35.0) [21.6; 5.5] |

* two of the patients with bilateral TFA were only treated on one leg each within the study. One was treated with the same method on the other side before the study started, and one could not be treated on the other side owing to an extremely short residual femur
† data missing for one patient who did not specify the amputation date
‡ data missing for one patient who did not specify weight
§ measured by CT scan from the distal tip of the femur to the apex of the major trochanter

**Table II.** Overview of inclusion and exclusion criteria

| Inclusion criteria | Exclusion criteria |
|---|---|
| Transfemoral amputee | Age < 20 years or > 70 years |
| Current problems or expected to have problems with a conventional prosthesis, or inability to use a prosthesis | Severe peripheral vascular disease, diabetes mellitus, skin disease involving the amputated limb, or other diseases that could adversely affect the treatment |
| Full skeletal maturity | Current treatment with systemic corticosteroids, chemotherapeutic agents or other drugs that could adversely affect the treatment |
| Normal skeletal anatomy | Pregnancy |
| Suitable for surgery based on medical history and physical examination | |
| Likely to comply with treatment and follow-up requirements | |

for the Rehabilitation of Amputees); Integrum AB, Mölndal, Sweden) consists of three main components: the fixture, the abutment and the abutment screw (Fig. 2). Treatment involves two operations separated by six months, followed by rehabilitation. The first stage consists of the fixture being inserted into the residual femoral bone, using a three-dimensional (3D) centring guide and fluoroscopy to ensure correct positioning. The intramedullary canal is reamed to the appropriate size and the fixture is introduced. It is left unloaded in the bone during the healing period in order to allow it to incorporate.[9] In the second stage, all distal muscles are divided and sutured to the periosteum, leaving the bare bone protruding by approximately 5 mm, covered only by part of the skin flap, which is trimmed of subcutaneous fat to full skin thickness and attached to the end of the bone.[10] The abutment is then inserted, penetrating through

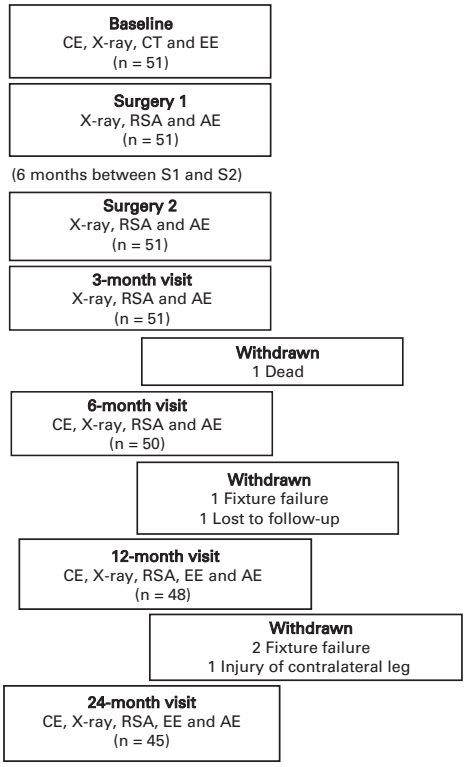


Fig. 1

Flowchart of the study design and patient participation over time (CE, clinical examination; X-ray, plain radiographs; CT, computed tomography; EE, Q-TFA Questionnaire for Persons with a Transfemoral Amputation; SF-36, Short Form 36 Health Survey; RSA, roentgen stereophotogrammetric analysis; AE, adverse event).

the skin into the implant, and secured with the abutment screw. Rehabilitation entails gradually increasing the load on the implant, mobilisation and activity.[11]

The patients were reviewed at three, six, 12 and 24 months after the second-stage procedure. Any complications were recorded. If there was clinical evidence of infection, additional information on the history of the infection and its treatment was recorded.

Two validated, self-reported questionnaires, the Questionnaire for Persons with Transfemoral Amputation (Q-TFA)[12] and the Short-Form 36 Health Survey (SF-36)[13], were used to assess the functional outcome and health-related quality of life. Both were completed before the first-stage procedure and 12 and 24 months after the second (Fig. 1).

The Q-TFA records scores in four areas: prosthetic use (0 to 100), prosthetic mobility (0 to 100), problems (100 to 0) and global (0 to 100). A prosthetic use score of 0 means that the prosthesis is not used at all, whereas 100 means that the prosthesis is used seven days a week for > 15 hours a day. The Q-TFA also includes a question on the patient's overall perception as an amputee, which can be evaluated regardless of the use of the prosthesis.[12]

The SF-36 is a general health-related quality of life questionnaire with eight subscales and two summary measures, and each gives a score between 0 and 100, with a higher figure representing better quality of life.[13,14] The summary measures and the physical and mental component scores, are standardised to the general population.[14]

The primary outcome of interest was the Q-TFA prosthetic use score; secondary outcomes included the remaining scores and the single overall question from the Q-TFA, and all scores on the SF-36.

**Statistical analysis**. All data, including any adverse events, were collected from the medical records and all statistical analyses were performed with the SAS (Statistical Analysis North Carolina) version 9.2, in accordance with a prespecified statistical plan. Descriptive statistics, including quantitative and qualitative parameters, were used for number of patients, mean, standard deviation (SD), median, minimum and maximum values and frequencies and percentages. Survival of the implant was calculated using a cumulative success rate (CSR) and presented as a Kaplan–Meier graph with 95% confidence intervals. Within-group tests were used for the time effect, i.e. evolution between pre- and post-treatment, using Wilcoxon's signed ranks non-parametric test. The significance tests were performed at subject level, two-sided, and conducted at the 5% significance level.

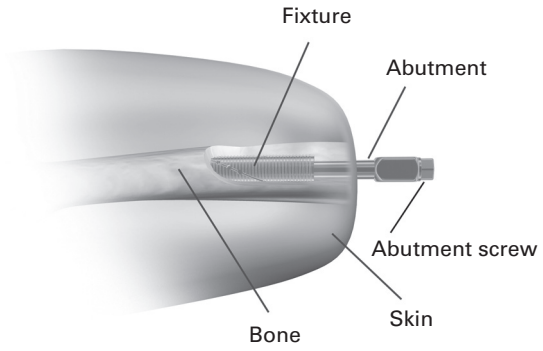


Fig. 2a

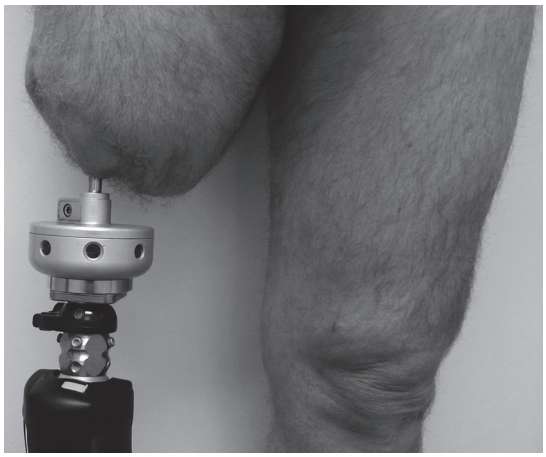

Fig. 2b

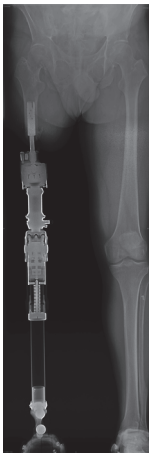

Fig. 2c

Figure 2a – schematic of the implant system. The fixture is inserted in the bone. The abutment is connected to the fixture and secured with an abutment screw. The external part of the abutment is connected to external prosthetic components. The fixture was manufactured from commercially pure titanium, had an outer thread, length 80 mm, and a diameter from 16 mm to 20 mm in increments of 0.5 mm, and in this study all implants had six tantalum markers for roentgen stereophotogrammetric analysis and radiological assessment reported separately.[37] Figures 2b and 2c – clinical photograph (b) showing a patient with the osseointegrated percutaneous implant, and radiograph (c) showing an osseointegrated implant with an attached external prosthesis.

## Results

A total of 48 of 51 patients (52 TFAs) were followed up for two years; three patients were withdrawn from the study for reasons unrelated to the implant (one death from an unrelated cause, one severe dysfunction of the contralateral knee, and one lost to follow-up). Three patients had their implants removed during the study period and one shortly after the study ended, and this failure is included in the results. The cumulative survival was therefore 92% after two years (95% CI 80% to 97%)(Fig. 3).

No patient suffered from any systemic events such as myocardial infarction or pulmonary embolism. A total of 46 patients (47 TFAs) had one or more (1 to 11) complications. A total of 101 complications were reported, and of these, 49 in 39 patients (39 TFAs) were classified as serious. Superficial infections were the most common complication occurring 41 times in 28 patients (29 TFAs), which were mainly treated effectively with oral antibiotics for ten days, although four patients required prolonged treatment. Four patients (four TFAs) with a superficial infection were admitted for treatment. All superficial infections resolved.

Four patients (four TFAs) had a deep infection, presenting at a time that varied from immediately after the first stage procedure to 42 days after the second stage. The deep infection in one patient led to loosening of the implant which was removed six months after the second-stage procedure. Another patient with a deep infection was successfully treated with antibiotics without removal of the implant. Two patients (two TFAs) had positive cultures from soft tissues taken at surgery (*E. coli* in one patient and *Pseudomonas aeruginosa* in the other), despite the absence of signs of infection. *E.coli* was treated with septacidin for

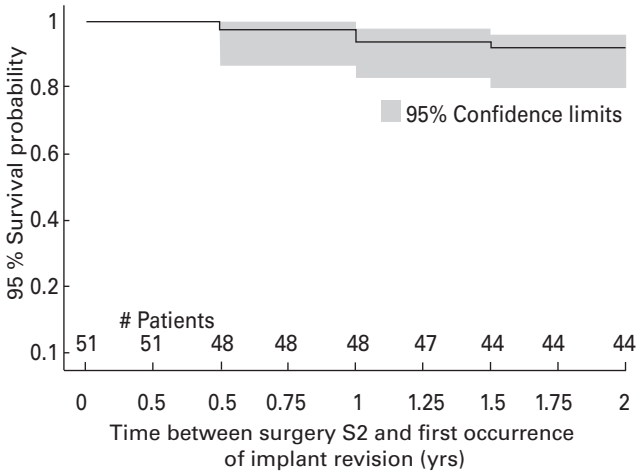


Fig. 3

Kaplan-Meier graph showing survival of implant with 95% confidence intervals.

10 days and then loracarbef for five months. *Pseudomonas* was treated with ciprofloxacin for six months, and neither developed clinical signs of infection.

Two patients with pain on weight-bearing had loose implants, which were removed 1.3 and 1.7 years after the S2, respectively. Another had almost constant pain on weight-bearing two years post-operatively, but loosening became apparent four months after the study was concluded. Five patients (five TFAs) described episodic pain during rehabilitation, but without evidence of loosening of the implant.

A total of four patients (four TFAs) suffered five fractures, three of which were ipsilateral fractures of the hip, one below-elbow fracture and one vertebral compression. No peri-prosthetic fractures occurred.

In all, nine mechanical complications with the abutment and/or the abutment screw were reported in four patients, resulting in fracture or bending of the abutment and/or the abutment screw. Six of these occurred in the same patient. All patients returned to normal function after the damaged components were replaced. There were no mechanical complications relating to the fixtures.

The Q-TFA and SF-36 scores are presented in Table III and are based on a patient level regardless of whether the patient had a unilateral or bilateral TFA. At 24 months 40 of 45 patients (89%) reported daily prosthesis use, compared with 57% (29 of 51) before the implant was inserted. One patient had severe pain and did not use the prosthesis at all, and four patients (two with bilateral TFA) reported less than daily prosthesis use, for different reasons. The mean prosthetic use score improved from 47 (0 to100) prior to the first stage to 79 (0 to 100) two years after the second stage procedure ($p < 0.0001$). As shown in Table III all Q-TFA scores improved ($p < 0.0001$) (Table III) from before the first stage, showing improved prosthetic mobility, fewer problems and an improved global situation. The overall situation as an amputee was stated to be improved in 31 (69%) of patients in the single question. The SF-36 physical function scores showed that general quality of life improved ($p < 0.0001$) (Table III).

In order to control for those who were lost to follow-up (n = 6), a sensitivity analysis, including all patients, was made using the primary functional outcome variable, the prosthetic use score, with a conservative estimate of their current prosthetic use at two years. The conservative analyse was based on baseline prosthetic use and personal contact. The results showed that the score was still statistically significantly improved (n = 51; mean change in prosthetic use score 26.1 (SD 43.5); $p < 0.0001$).

## Discussion

This is the first prospective study analysing quality of life, function and complications following the use of an osseointegrated percutaneous prosthetic implant for the treatment of patients with TFA. We found a cumulative survival of 92% two years post-operatively, which is in contrast to previous reports of direct skeletal attachment for prostheses, which in dogs and goats have shown limited prosthetic function owing to implant loosening or infection or only been used for almost unloaded implants in humans.[15-17]

Brånemark[9] introduced the concept of osseointegration, which has revolutionised dental treatment[18,19] and has also been used successfully for hearing aids,[6] craniofacial prostheses[7] and thumb prostheses.[8] Using this concept for patients with TFA is a continuation of this development. A report from a German concept for percutaneous prostheses fixed to bone of transfemoral amputees have shown promising results, although still lacking prospective short and medium follow-up regarding implant survival, infection rates and rate of revision.[20] In 37 patients who have undergone arm amputations at various levels and been treated with implants during 1990-2010, 30 patients continued to successfully use the implant and a case report using the British osseocutaneous ITAP system in a patient with transhumeral amputation has survived two years without any reported signs of serious complications.[21,22]

There are a large number of lower limb amputees worldwide; many are young, and TFA prostheses traditionally have used suspended sockets.[23-25] However, problems with the socket are common because of poor suspension and fit, local pain, skin ulceration and general discomfort.[1-3,26,27] Patients with a short stump or inadequate soft tissues may choose not to use their prosthesis at all.[4] In a survey of Vietnam war veterans with amputations in the USA, Hoaglund et al[2] reported a high incidence of persistent discomfort. In Sweden, a survey of 97 patients with TFA reported that 72% experienced heat and sweating of the stump; 62% had sores/chafing/skin irritation; 61% had interference with mobility; 51% had pain in the stump when standing or walking; and 44% were uncomfortable sitting with the prosthesis. In addition, the patients had significantly

**Table III.** Questionnaire for Persons with a Transfemoral Amputation (Q-TFA) and Short-Form (SF)-36 scores at baseline and change from baseline to 12- and to 24-month follow-up, respectively. Three patients failed to complete the whole questionnaire at each visit

| | Mean score (range ) [median; SD] (no. patients) | | |
|---|---|---|---|
| **Variable** | **Baseline** | **Change from baseline to 12 mths** | **Change from baseline to 24 mths** |
| **Q-TFA*** | | | |
| Prosthetic use score | 47 (0 to 100) [52; 37] (n = 51) | 34 (-23 to 100) [29; 29] (n = 44)§ | 32 (-100 to 100) [29; 41] (n = 45)§ |
| Prosthetic mobility score | 52 (0 to 82) [56; 20] (n = 42) | 14 (-29 to 46) [15; 17] (n = 36)§ | 18 (-29 to 48) [17; 16] (n = 37)§ |
| Problem score† | 44 (5 to 77) [48; 19] (n = 42) | -28 (-57 to 2) [-33; 16] (n = 36)§ | -27 (-59 to 7) [-30; 16] (n = 37)§ |
| Global score | 38 (0 to 92) [33; 19] (n = 42) | 37 (-17 to 84) [34; 26] (n = 36)§ | 39 (0 to 92) [34; 24] (n = 37)§ |
| Overall situation (n, %) | | | |
| Extremely poor | 5 (*10*) | n = 42 | n = 45 |
| Poor | 15 (*29*) | Declined: 2 (*5*) | Declined: 3 (*7*) |
| Average | 17 (*33*) | No change: 11 (*26*) | No change: 11 (*24*) |
| Good | 9 (*18*) | Improved: 29 (*69*)§ | Improved: 31 (*69*)§ |
| Extremely good | 5 (*10*) | | |
| SF-36 | | | |
| Physical function | 35 (0 to 85) [30; 22] (n = 51) | 22 (-40 to 70) [20; 24] (n = 47)§ | 23 (-23 to 75) [25; 21] (n = 45)§ |
| Role-physical | 41 (0 to 100) [25; 42] (n = 50) | 24 (-50 to 100) [25; 44] (n = 45)§ | 22 (-50 to 100) [13; 36] (n = 44)§ |
| Bodily pain | 55 (10 to 100) [51; 26] (n = 51) | 7 (-52 to 74) [0; 26] (n = 47) | 6 (-61 to 59) [9; 30] (n = 45) |
| General health | 78 (37 to 100) [82; 18] (n = 51) | 3 (-32 to 40) [0; 17] (n = 47) | -1 (-42 to 40) [0; 18] (n = 45) |
| Vitality | 60 (15 to 90) [60; 20] (n = 51) | 5 (-50 to 45) [5; 19] (n = 47) | 3 (-70 to 45) [5; 23] (n = 45) |
| Social function | 78 (13 to 100) [88; 25] (n = 51) | 2 (-50 to 50) [0; 24] (n = 47) | 1 (-100 to 63) [0; 30] (n = 45) |
| Role-emotional | 75 (0 to 100) [100; 39] (n = 50) | 5 (0 to 100) [0; 43] (n = 46) | 0 (0 to 100) [0; 45] (n = 44) |
| Mental health | 74 (4 to 100) [80; 21] (n = 51) | 2 (-44 to 40) [0; 18] (n = 47) | 2 (-76 to 40) [4; 24] (n = 45) |
| SF-36 Physical Component Summary‡ | 74 (4 to 100) [80; 21] (n = 50) | 2 (-44 to 40) [0; 18] (n = 45)§ | 2 (-76 to 40) [4; 24] (n = 44)§ |
| SF-36 Mental Component Summary‡ | 53 (19 to 69) [57; 13] (n = 50) | -2 (-33 to 23) [-2; 11] (n = 45) | -3 (-44 to 22) [0; 15] (n = 44) |

* a Prosthetic Use Score of 0 means the patient is not using a prosthesis and consequently the Prosthetic Mobility Score, Problem Score and Global Score could not be answered, hence results for lower numbers of patients in those scores[1]
† the Problem Score is reversed, which means a lower figure indicates fewer problems related to amputation and prosthesis
‡ SF-36 Physical and Mental Component Summaries are normalised to the general population (mean 50 (SD 10))[13]
§ $p < 0.001$

reduced quality of life compared with matched controls (normal subjects), with the greatest differences in the SF-36 physical function scores.[1] The prosthetic socket has also been shown to hinder the movements of the hip.[28] Osseointegrated implants are a novel addition to the growing number of mucosa- and skin-penetrating implants. These devices not only allow for fixation of the components to bone, they also create new opportunities for the exchange of information between the prosthesis and the rest of the body, using vibration, epimysial electrodes (surgically placed on the muscle to record the electrical signal from the muscle contraction) and nerve cuff electrodes.[29-31] The latter can improve the use of the advanced upper limb prostheses recently developed by the Defence Advanced Research Projects Agency and could be used in conjunction with other advanced rehabilitation techniques, such as targeted muscle reinnervation.[32]

An early major concern with the use of skin- or mucosa-penetrating devices, which are anchored to bone, is the risk of infection. However, long-term studies have shown that osseointegrated dental implants can last for > 20 years, with few complications.[18,19] In a recent study of 39 amputees treated with osseointegrated percutaneous implants, the patients have lived with the implants for a mean of 56 months (132 to 133). There were 33 femoral, one tibial, four ulnar, four radial and three humeral implants. Patients were selected during a six month period in 2005 and identically re-evaluated after three years. The frequency of implant infection was 5% at inclusion and 18% at follow-up. One patient with infection recovered owing to antibiotic treatment and another patient had the implant removed. Most implant infections had low infectious activity and in five of the seven patients with infections, prosthetic use was not affected. Tillander et al[33] reported that, despite frequent colonisation around the skin–implant interface by potentially virulent bacteria, e.g. *Staphylococcus aureus* or coagulase-negative staphylococci, few infections lead to disability or removal of the implant. Furthermore, in animal studies it has been suggested that osseointegrated implants can remain stable despite inflammatory conditions; inflammation is a part of the response to infection and we hypothesise that the resistance to inflammation is a key factor in the resistance to infection.[34]

We have previously reported improved prosthetic use, improved mobility, less problems and improved health-related quality of life of osseointegrated implants in a subanalysis of the first 18 patients included in this study.[35] Moreover, the results are supported by Lundberg et al[36] in

a qualitative study that included 13 patients with osseointegrated prostheses who described the 'revolutionary change' this treatment made to their lives.

In this further study we found no superficial infection that developed into a deep infection, and no patient had a persistent deep infection. The incidence of revision requiring removal of the implant was relatively low (8%). The limitations of this study are that the number of patients (n = 51) (55 TFAs) was small, and that the two-year follow-up data for six patients (six TFAs) were not available. The study was not randomised, nor was it multicentre, and the follow up was short. However, based on our 20 years' experience of using this implant, early loosening is the most common complication requiring removal of the implant. The five-year data are currently being assessed and will be reported shortly. Also, the first patients have passed the ten-year follow-up, and to date there are no late implant failures due to loosening or infection. However, one implant was removed after ten years because of a crack in the fixture, probably caused by mechanical overload. The radiological assessment of this cohort has been published, indicating that these implants behave in a similar way to femoral stems in total hip replacement.[37] In future, it is hoped that these novel percutaneous devices will not only allow improved fixation of prostheses, but may also help deliver information between the artificial components and other systems within the body.

## Supplementary material

A table detailing all adverse events encountered during the study is available with the electronic version of this article on our website www.bjj.boneandjoint.org.uk. A further opinion by R. Grimer is available with the electronic version of this article on our website at www.boneandjoint.org.uk/site/education/further_op

## Supplementary video

Two videos demonstrating this system are available with the electronic version of this article.

RB is part time employed by the Integrum company.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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