Patient-Specific Implants for Focal Cartilage Lesions in The Knee: Implant Survivorship Analysis up to Seven Years Post-Implantation

Leif Ryd, MD
Senior Medical Consultant
Episurf Medical
Stockholm, Sweden

Katarina Flodström, PhD
Chief Scientific Officer
Episurf Medical
Stockholm, Sweden

Michael T. Manley, FRSA, PhD
Consultant in Orthopaedic Sciences
Michael T. Manley FRSA, PhD, LLC
Naples, FL, USA

ABSTRACT

In the quest for increased surgical precision and improved joint kinematics, Computer-Assisted Orthopedic Surgery (CAOS) shows promising results for both total and partial joint replacement. In the knee, computer-assisted joint design can now be applied to the treatment of younger patients suffering pain and restriction of activity due to focal defects in their femoral articular cartilage. By taking MRI scans of the affected knee and digitally segmenting these scans, we can identify and map focal defects in cartilage and bone. Metallic implants matched to the defect can be fabricated, and guide instrumentation to ensure proper implant alignment and depth of recession in the surrounding cartilage can be designed from segmented MRI scans.

Beginning in 2012, a series of 682 patient-specific implants were designed based on MRI analysis of femoral cartilage focal defects, and implanted in 612 knees. A Kaplan-Meier analysis found a cumulative survivorship of 96% at 7-year follow-up from the first implantation. Fourteen (2.3%) of these implants required revision due to disease progression, incorrect implant positioning, and inadequate lesion coverage at the time of surgery.

These survivorship data compare favorably with all other modes of treatment for femoral focal cartilage lesions and support the use of patient-specific implants designed from segmented MRI scans in these cases.

INTRODUCTION

Sophisticated computerized methods of implant design and placement have become increasingly common in the field of orthopedics. Computer-Assisted Orthopedic Surgery (CAOS) has been shown to be effective in reducing the number of outliers that occur with traditional methods of knee alignment and component placement following total knee arthroplasty (TKA).[1-3] In advanced systems, computer models of the diseased knee are produced pre-operatively from MRI or CT scans and used to develop a specific pre-operative plan. During surgery, stereo cameras monitor the movement of the patient and instru-

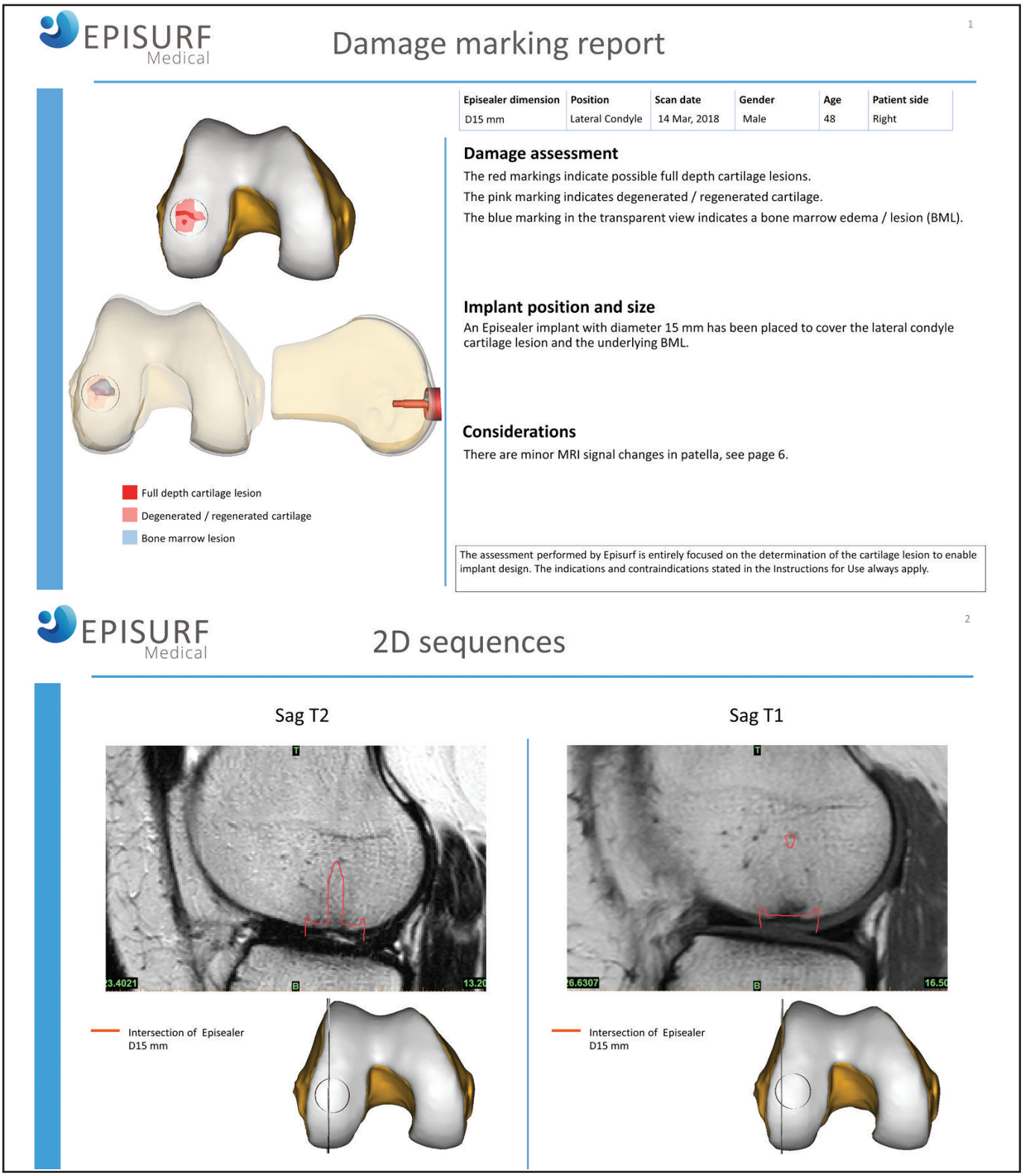

Figure 1. A Damage Marking Report (DMR) showing a partial-depth cartilage lesion (pink), a full-depth cartilage lesion (red), and an underlying bone marrow lesion (blue). The two MR images correspond to the lesions described in the DMR.

ments so that the pre-operative plan can be followed with precision. In some systems, patient-specific guide saw blocks developed from pre-operative knee images, so-called PSI-TKA technology, show improved component alignment compared to alignment with traditional cutting guides.[4,5] In an extended application of CAOS, patient-specific total knee implants, developed pre-operatively from MR images, have been suggested to be a way to completely individualize knee surgery. Superior component fit and alignment[6,7] and excellent clinical performance have been reported.[8]

Younger patients with focal lesions in the femoral articular cartilage of the knee are not usually regarded as candidates for TKA, even though they may suffer pain, restricted range of motion, and difficulty participating in sports or other activities.[9] If left untreated, focal lesions are regarded as a precursor to severe knee osteoarthritis (OA).[10-14] Methods for treating focal defects include microfracture of the bone bed underlying the lesion to generate fibrocartilage,[15] restoration of normal hyaline cartilage in the lesion by chondrocyte implantation,[16-18] and filling of the defect by cartilage resurfacing implants.[15,19] Results obtained with autogenous chondrocyte implantation (ACI), developed in the 1990s by Brittberg and coworkers,[17] suggest that cell implantation successfully relieves pain and restores function in patients up to age 35-40 years.[20-23] Microfracture has been shown to be effective in younger patients with small lesions.[24] A disadvantage with both microfracture and chondrocyte implantation is that extensive periods of restricted weight-bearing following surgery are required to protect the repair.[25] Also, these biological methods do less well in patients older than 30-35 years.[26-29]

Small metallic implants, developed in the last decade,[26-28, 30] may be a way to treat patients who are too old for biological treatment and too young for TKA, the so-called GAP-age.[31] Metallic implants have the benefit that the defect is filled immediately and the surrounding healthy cartilage receives structural support to prevent defect enlargement.[32] Patient rehabilitation is thus much shorter than with biologic treatments. One caveat learned from animal studies is that exact sizing and placement of a metallic implant is important. The fit of the prosthetic articular surface with the surrounding healthy cartilage must minimize synovial fluid intrusion into the interface between the implant and subchondral bone to protect fixation.[17] In addition, the metallic articular surface must be slightly recessed below the surrounding healthy femoral cartilage to minimize wear of the opposing (tibia or patella) cartilage counterface.[33]

A first-generation metallic focal defect implant (HemiCAP/UniCAP, Arthrosurface, Boston, MA, USA) featured a library of different articular surface shapes in an attempt to provide a "best-fit" to a focal lesion during surgery. Pain relief and restoration of function were reported for patients with implants sized and implanted properly. When implants were misplaced or left proud of the cartilage surrounding the defect, erosion of the opposing articular surfaces was seen.[34,35]

A more recent development (Episealer, Episurf Medical, Stockholm, Sweden) uses the CAOS approach in the design of patient-specific focal defect-filling implants and associated instrumentation. This technology uses segmented MR images for lesion analysis, 3D-reconstruction of the knee in computer models developed from the segmented images, and computer-aided design and manufacturing for the implant and associated instruments.[36,37] Patient rehabilitation time to full weight-bearing has been shown to be about 6 to 8 weeks, with excellent short-term pain relief and survivorship.[38,39] An important measure of the success of this approach is implant survivorship, since the return of pain will normally lead to implant removal. We report here a survivorship analysis of the first 612 knees (682 patient-specific implants) treated with this technology over the first eight years of clinical use. We also report all complications found.

MATERIALS AND METHODS

For each patient who was a candidate for the Episealer technology, a three-dimensional MRI sequence of the damaged knee was taken and uploaded to the manufacturer. The MRI images were anonymized in the uploading process and only patient age and gender were included as a coarse identity safeguard. A radiologist reviewed all MRI scans to ensure that the knee was a candidate for focal defect-filling, and the scan was segmented digitally. A three-dimensional model of the knee with defects and surrounding cartilage was produced (Fig. 1). A Damage Marking Report (DMR) describing the knee pathology was generated and a custom plan with details of the implant design and the implant position required to fill the defect was developed. Possible contraindications for the procedure, such as excessive cartilage wear in the femur or wear of the opposing cartilage on the tibia and/or patella, as well as severe osteo-arthritis were identified at this stage and integrated in the DMR (Fig. 1). The entire DMR was uploaded for approval by the treating surgeon. If the surgeon approved the patient treatment plan, the implant and instruments were manufactured.

Implant design parameters included a patient-matched articulating surface, as well as full coverage of the defect to ensure contact between the implant and surrounding cartilage. Implants were manufactured from cobalt-chromium alloy to provide an articulation that is resistant to wear. For the fixation interface, the alloy was coated with titanium and hydroxyapatite to encourage biologic fixation in subchondral bone. To ensure the necessary precision at surgery, each implant was matched with individualized guide instruments to ensure proper positioning of the implant and its recession below the surrounding cartilage.

For the surgical procedure, the implant was delivered with a visualization guide that showed details of the final design and its required surgical placement (Fig. 2).[37]

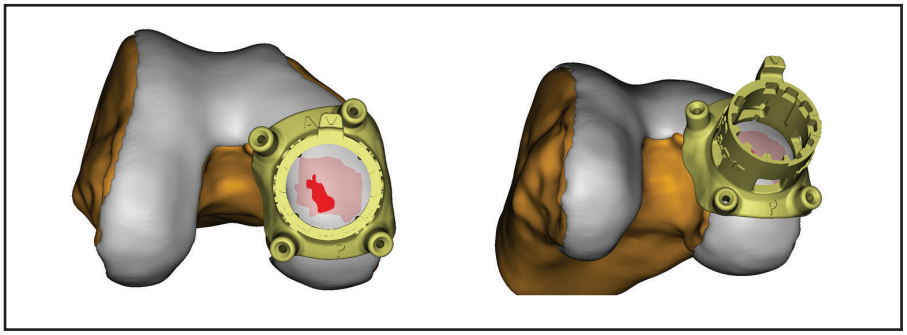

Figure 2. Examples from a "Final Design". The shape and position of the MRI-based individualized 3D-printed guide instrument are shown.

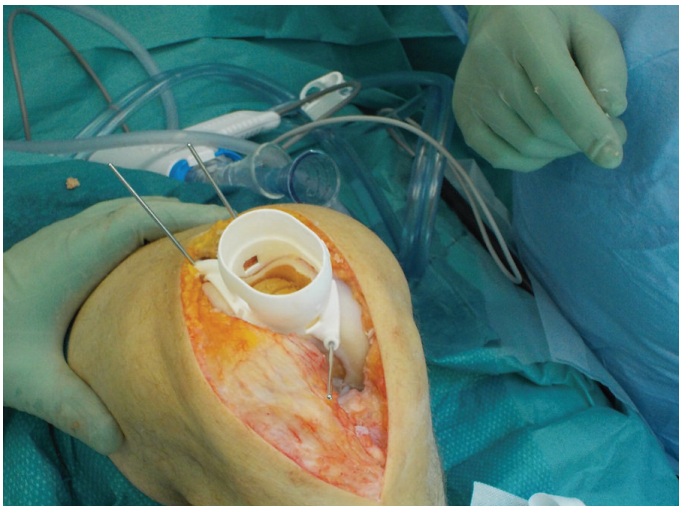

Figure 3. Patient-specific alignment guide to ensure accurate positioning of the implant.

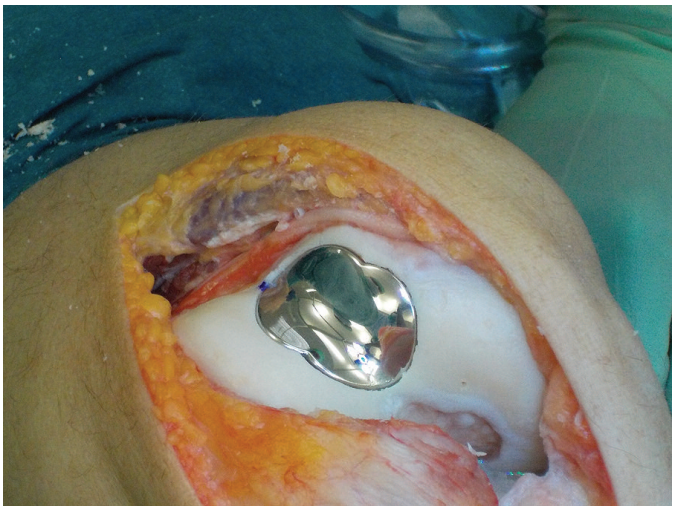

Figure 4. A patient-specific implant placed with custom instrumentation. Note the recession of the implant beneath the level of the surrounding cartilage. (Courtesy T. Spalding, MD)

Implantation was performed using the patient-specific instrumentation guide (Fig. 3). A drill guide located on the cartilage surrounding the defect and a depth gauge allowed fine-tuning of the drill depth in increments of 200 µm. The required recession of the implant articulation was checked using a dummy to ensure that the articular surface of the implant was approximately 0.5 mm below the surrounding healthy cartilage (Fig. 4).

For the survival analysis reported here, we examined all post market surveillance records from all patients in the database held by the manufacturer without any exclusions. This analysis included all implants that required revision for any cause. Patients treated from December 2012 (first implantation) to the end of June 2020 were included in the analysis. Revisions were tabulated and the reasons for revision were recorded in the adverse event analysis file. The cause of revision was analyzed for each case, and the original DMR and treatment plan were reviewed.

Survivorship was calculated using a Kaplan-Meier analysis.[40] To calculate the cumulative revision rate (CRR), the number of knees "at risk" of revision at the beginning of each year of follow-up was determined. The number of revisions during each year of follow-up was registered and divided by the numbers "at risk" during that period and expressed as a percentage. These yearly percentages were added together to give a cumulative revision rate.

Table I
Revisions Reported at 7-year Follow-Up

Case	FU at revision (months)	Age (at index op)	Site	Implant type	Revision Cause
1	6	39	Trochlea	Solo	Other pain (fem-tib OA)
2	7	44	Trochlea	Solo	Trauma 3 weeks post-op
3	8	65	Med condyle	Twin	Disease progression, possibly related to technical error at operation
4	11	43	Med condyle	Twin	Unknown pain. Metal allergy, unknown relevance
5	15	45	Med condyle	Twin	Pain, several lesions in the knee.
6	16	61	Med condyle	Solo	Borderline indication. Tibial cartilage wear
7	19	32	Med condyle	Twin	Pain, proud implant
8	28	52	Lat condyle	Solo	Infection
9	28	52	Med condyle	Twin	Unknown, revised by another surgeon
10	30	52	Med condyle	Solo	Lesion was too large, not fully covered by the implant
11	28	50	Trochlea	Twin	Other pain (fem-tib OA)
12	29	55	Med condyle	Twin	Pain. Other lesions in the knee at the time of surgery, occurred after the DMR.
13	30	42	Trochlea	Solo	Additional HTO failed
14	30	38	Trochlea	Solo	Implant was too small, lesion not fully covered. Progression of lesion after surgery

OA, osteoarthritis; DMR, Damage Marking Report; HTO, high tibial osteotomy

Table II
Cumulative revision of 612 Episealer (Episurf Medical, Stockholm, Sweden) knees at 7-year follow-up

Time (months)	Number at Risk	Cumulative Number at Risk	Failure			Survival		
			Estimate	95% LB	95% UB	Estimate	95% LB	95% UB
0	612	--	--	--	--	--	--	--
12	478	4	0.75%	0.28%	1.99%	99.25%	98.02%	99.72%
24	327	7	1.43%	0.68%	2.99%	98.57%	97.01%	99.32%
36	191	14	4.05%	2.36%	6.92%	95.95%	93.08%	97.64%
48	97	14	4.05%	2.36%	6.92%	95.95%	93.08%	97.64%
60	42	14	4.05%	2.36%	6.92%	95.95%	93.08%	97.64%
72	15	14	4.05%	2.36%	6.92%	95.95%	93.08%	97.64%
84	4	14	4.05%	2.36%	6.92%	95.95%	93.08%	97.64%

RESULTS

During the evaluation period, a total of 682 Episealer implants were implanted in 612 knees. The patient age at surgery ranged from 27 to 72 years, with a mean value of 48.6 years. One patient operated upon in 2018 died from unrelated causes in 2019, but has been included in the calculations.

At the time of this writing, 14 of the 612 operated knees have been revised. This corresponds to a crude revision rate of 2.3%. The revisions and the reasons for each are shown in Table I.

Revisions were due to various causes, that included disease progression, incorrect implant positioning, inadequate lesion coverage and causes unrelated to the implant. In three revised cases, the pre-operative indications were poor as there were additional lesions in these knees that were not treated. In one case, there was a technical error at implantation and in three cases manufacture of the implant was slightly different than that described in the DMR. There was one case of infection. Revisions included eight implants placed in the medial condyle, one in the lateral condyle and five in the trochlea area. For knees receiving multiple implants, there were no revisions within the study period. A Kaplan-Meier survivorship analysis of the patients at risk at the beginning of each year of follow-up is shown in Table II. Kaplan-Meier survivorship at six years of follow-up was 96.3% (Fig. 5). This value includes revision due to all causes.

DISCUSSION

Computer-Assisted Orthopedic Surgery (CAOS) for joint replacement in the knee has included precision monitoring of cutting angles through the monitoring of saw and patient movement[1,41] as well as patient-specific cutting blocks and patient-specific total knee implants.[5-7] It has been suggested that these systems come with a learning curve, add time to the operative procedure, and are not yet fully accepted.[2,3,42]. From a technological perspective, proponents claim improved accuracy of implantation [4,6,7,43] and better functionality in the mid-term follow-up.[8] However, a recent Cochrane analysis reported no difference in accuracy with some of these approaches compared to standard implantation systems.[44] The jury is still out on the use of CAOS for total knee replacement.

Accurate resurfacing of focal defects in the articular cartilage in the femoral knee can only be attempted with computer-aided design and manufacture. Each defect is unique with respect to size and extent, while accurate implant placement is crucial to procedural effectiveness. Excellent clinical results in terms of

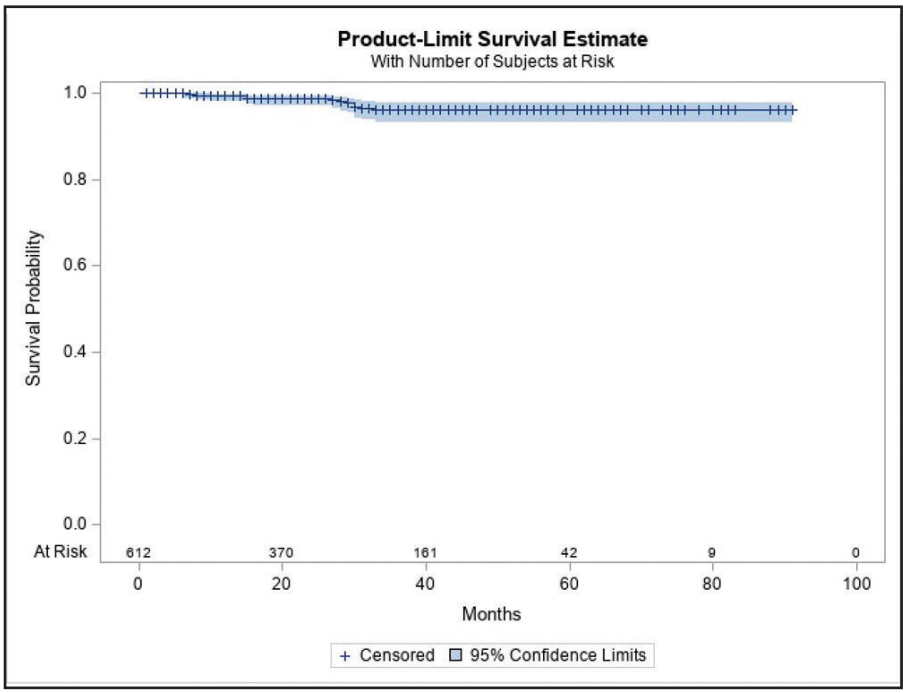

Figure 5. Cumulative survival graph of 612 patients receiving 682 patient-specific focal defect resurfacing implants.

patient-reported outcome measures (PROMs) have recently been reported for patient-specific focal defect knee implants at two years post-implantation.[29,38] The procedure was reported to be simple and reproducible and good relief of pain was achieved.[38] In a series of 80 implants, 2.5 % had been revised at 24-months follow-up. We have shown here, in a larger series of 682 implants, that survivorship at 7-years follow-up was better than 96%. There were 14 revisions out of the 682 implants placed, with a crude revision rate of 2.5%.

These survival results are superior to those reported for other surgical approaches to this type of lesion; survival data for microfracture, non-custom metal implants and ACI indicate a survival rate of about 75% at 6 years after implantation.[45-47]

Joint replacement registries are an increasingly important source of survivorship data. Large numbers of entries provide statistical power, but necessitate the use of simple analysis such as survival statistics.[48] For reasons of statistical power, we chose survival data as the dependent variable in our report. Recent survival analyses of focal defect resurfacing implants available in the Australian Joint Arthroplasty Registry show a 6-year survival of about 75% and an 11-year survival of 54% for 244 first-generation metal resurfacing devices implanted.[34] The Australian Registry reported that the most common mode of failure for a metal defect resurfacing implant was "progression of the joint disease", perhaps an osteoarthritic process, an ill-fitting device and/or liberal preoperative indications. By comparison, the survivorship of 96% found in our analysis mimics the best TKA survivorship reported in national registries, albeit for older, less-active patients.[34,49]

Perhaps it is reasonable to assume that the superior results we report here are due to the patient-specificity of implants and instruments. In animal studies, an implant that is designed to accurately fill the defect was shown to protect the integrity of fixation from damage due to synovial fluid intrusion into the supporting subchondral bone. The titanium/hydroxyapatite coating of the implant also promotes adherence of cartilage, so-called chondro-integration,[50] further protecting fixation. For longevity of the articulation, a metallic implant must not protrude above the surrounding cartilage or it will severely damage the opposing cartilage counterface.[33,51]. The incremental fine-tuning allowed during drilling by the patient-specific alignment guides ensures that implants are neither tilted nor inserted in a too-shallow position. Human cartilage compresses asymptotically upon weight-bearing by about 20%,[52] corresponding to about 0.5 mm in the normal knee. For patients with these metallic implants, activities such as walking or running will compress the joint space and cause the opposing cartilage to meet metal. The key to survival is proper implant positioning so that, during joint compression, the opposing cartilage does not meet a metal edge. A contraindication for this procedure is already-compromised opposing tibial cartilage found at the time of the preoperative DMR.[46] Thus, for the Episealer technology, opposing cartilage ICRS stage III-IV is a contraindication and such patients are usually not accepted for surgery.

Of the 14 revisions in this report, three (patients 2, 3 and 8 in Table I) were caused by factors that could not be attributed to the index surgery.

In two cases (patients 10 and 14), the implant did not cover the entire cartilage lesion. Often, lesions are extremely irregular in shape, with "corners" sticking out some distance from the core lesion. To accommodate such corners, a larger implant is needed, with excessive healthy cartilage excised. The DMR shows the shape of the lesion, and the surgeon must decide how best to balance implant size, placement, and lesion coverage. A smaller implant may mean that a portion of the cartilage lesion is left uncovered. It is known that small cartilage lesions can heal with time[53] but further work is required to analyze lesions that are not fully covered because of shape or due to their position close to the edges of the knee. Revision case 10 is an example of an edge lesion. The literature suggests that lesion size is inversely related to implant longevity,[35] and a longitudinal (A-P) size of 30-35 mm has been suggested as a contraindication for this approach. Somewhat surprisingly, we found that none of the larger Episealer implants with a length of 35mm were revised at the time of this analysis. One Episealer implant that was malplaced above the cartilage surface was revised for pain. Another three patients reported pain, and their implants were also revised. Pain as a complication is found following surgery of the knee and other joints. For focal defect implants, pain may be related to implant malposition or may be due to unknown cartilage conditions that are not resolved by these implants.

The use of MRI to evaluate a cartilage defect means that, as part of preoperative planning, both the cartilage and the subchondral bone can be assessed, visualized and used in establishing the indication for the procedure. Insufficient bone stock to support the implant and signs of severe progressive osteoarthritis are contraindications for treating the defect in isolation. MRI plays an important role in identifying and quantifying bone marrow lesions (BML).[54,55] Cartilage does not contain nerve-endings, but subchondral bone does. With patient-specific implants, BMLs can be identified and treated by excision and a corresponding thickening of the implant, with good relief from pain.[28]

In the treatment of full-thickness focal defects in the articular cartilage of the knee, microfracture and treatment by implantation of chondrocytes both show satisfactory results in the relief of pain and restoration of function. For a younger adult with a focal lesion, one of the primary patient needs is a short period of rehabilitation and a rapid return to full function. Neither microfracture nor a biologic approach meet this criterion as tissue growth and maturation may extend beyond 18 months post-surgery.[56,57] Metallic and polymeric implants that are used to fill cartilage defects do not require long periods of rehabilitation and a recovery of three months or so is often adequate for full functional activity to begin.[56,57] The literature shows that, with proper design, implantation technique and alignment, metallic implants can provide satisfactory clinical results and good patient satisfaction with a focal defect resurfacing procedure.[26-29,58]

CONCLUSION

In this follow-up of 612 consecutive patients (682 implants) receiving focal defect resurfacing implants for painful femoral cartilage defects, we have shown a 96% implant survivorship at 7 years post-implantation. Although survivorship by itself does not imply patient satisfaction with the procedure, these results

are superior to those reported in the literature for other focal defect-filling technologies. Of the 14 identified revisions in this analysis, none were due to a failing implant and most were due to improper patient selection. Review of the MRI scans of the implants that failed shows that, in some cases, the cartilage lesion was too large in both size and depth for resurfacing to be successful. The presence of osteophytes or adverse changes in bone density that may affect implant stability are now also known to be a contraindication for resurfacing. The careful assessment of the pathology of each individual patient should be considered when offering patient-specific implants as a solution to a painful femoral cartilage defect. However, for patients who satisfy the selection criteria, this technology offers a short rehabilitation time and the potential for long-term relief of pain and return of function in what would otherwise be a painful knee. STI

AUTHORS' DISCLOSURES

Dr Ryd is the Senior Medical Consultant to Episurf Medical AB (Stockholm, Sweden) and is compensated by the company for his work with them. Dr Flodstrom is Chief Scientific Officer of Episurf Medical AB and is an Episurf employee. Dr Manley is a consultant to Episurf Medical, Stryker Orthopaedics (Kalamazoo, MI) and other companies as need arises.

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