

## Posterior Cruciate Mechanoreceptors in Osteoarthritic and Cruciate-retaining TKA Retrievals: A Pilot Study

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### Abstract

**Background** Although normal cruciate ligaments and those in patients with osteoarthritic (OA) knees contain mechanoreceptors, it is unclear whether they are present after functioning in a cruciate-retaining total knee arthroplasty (TKA). **Questions/purposes** We therefore determined if the areas occupied by mechanoreceptors in the human posterior cruciate ligament (PCL) are similar in patients with osteoarthritis and in patients who have had TKA with retention of the PCL.

**Methods** We identified five cruciate-retaining TKA specimens from a retrieval program and obtained five PCLs during cruciate-sacrificing TKA from patients with OA; the

retrieved specimens had been in place 5 to 12 years. The whole en bloc PCL specimens were harvested for the study. These specimens were then sectioned to a thickness of 8 µm and mounted on microscope slides. Two transverse cross-sections from the distal third from each specimen 100 µm apart were then subjected to immunohistochemistry with neurofilament protein (NFP) and S-100 protein. **Results** All five PCL specimens in each group revealed multiple areas of positive stained elements with both S-100 protein and NFP immunohistochemical staining. Morphologically, these elements appear to correspond to Pacinilike, Golgilike, and fusiform types of mechanoreceptors. We observed no difference in positive staining mechanoreceptor elements as a percentage of area in the osteoarthritis and TKA groups.

**Conclusion** Mechanoreceptors appear to occupy similar areas before and after implantation of a TKA.

**Clinical Relevance** If mechanoreceptors continue to function after cruciate-retaining TKA, then it may continue to participate in proprioception of the knee after TKA.

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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### Introduction

The role of human knee ligaments is not just to provide mechanical support, but to also give feedback to the body to aid in dynamic stability [11, 18]. Ligaments consist of collagen fibers that act as a structural support but also contain neural elements that aid in their integration into the musculoskeletal system as a whole [4]. These neural innervations of ligaments use mechanoreceptors as a hardwire sensor to relay information about the mechanical state of the ligament. Mechanoreceptors are neurons that send afferent messages to the central nervous system, initiating efferent signals that keep a person from potentially

injurious action to the joint in which they function [7]. The presence of mechanoreceptors in the cruciate ligaments of the knee is well established [5, 7, 20, 22, 23]. They function to aid in the proprioception of the knee and in dynamic stability during activity. Their numbers are reduced in osteoarthritis [7, 22]. Whether and how they might function after performing a cruciate-retaining TKA has not been clearly determined [1, 2, 10, 13, 16, 23].

Retention or substitution of the posterior cruciate ligament (PCL) in primary TKA has been debated for years. Several reports suggest PCL retention after TKA may give better proprioception of the knee [9, 17], but others have shown no difference in proprioception measured by the difference in perceived and measured flexion angle error between cruciate-retaining (CR) and substituting designed TKA implants [13, 24]. Other histologic investigations of the PCL in osteoarthritic knees have revealed degenerative myxoid changes and the presence of all encapsulated and nonencapsulated types of mechanoreceptors [5, 21, 22]. A case report of one retrieved CR TKA reported the findings of mechanoreceptors using immunohistochemistry [14]. Although the fact that mechanoreceptors are reported in osteoarthritic (OA) PCLs, there is no evidence that the mechanoreceptors will persist after performing a CR TKA. If the mechanoreceptors remain, then we might not look for or understand their clinical importance after a TKA.

We therefore determined the presence and area of mechanoreceptors of PCLs after they have functioned in a CR TKA compared with PCLs retrieved in OA knees during primary posterior-stabilized TKA.

## Materials and Methods

The local retrieval program at the Medical Education and Research Institute (Memphis, TN, USA) is based in our laboratory and was the source the specimens in this case study. This program is based on donations and receives more than 700 donations per year of which 10% on average have undergone a TKA and/or THA during their lifetime. Using fluoroscopy we identified five CR TKA specimens and obtained whole en bloc knee specimens (Fig. 1). The TKAs from these five specimens had been in place from 5 to 12 years. Five PCLs were then obtained from patients undergoing a posterior-stabilized TKA from the operating room after informed consent was obtained. All OA knees had a varus deformity under  $10^\circ$  and no flexion contracture existed over  $10^\circ$ . During surgery, the PCL was sharply dissected off of the medial femoral condyle within the intercondylar notch. The PCL was then bluntly dissected with Metzenbaum-type scissors to the insertion at the posterior aspect of the midportion of the tibia. The PCLs were then transected at the joint line. Based on a manual posterior



**Fig. 1** The PCL in the retrieved specimen was intact and supportive of a posterior drawer when the specimen was tested manually.



**Fig. 2** Polyethylene insert from one of the retrieved cruciate-retaining TKA specimens with wear on the anterior half of the medial side of the insert indicating that posterior rollback is compromised in this case.

drawer test as performed at necropsy or during surgery, all TKA retrieval PCLs and OA PCLs were presumed to be normally functioning. All of the retrievals were believed to be adequately balanced on the medial and lateral sides of the joints as assessed by manual varus and valgus-applied stress. The polyethylene inserts in the CR TKAs all showed evidence of roll-forward wear patterns on the medial aspect (Fig. 2) [6, 25]. We had prior Institutional Review Board approval before the study was undertaken.

We placed all the PCLs in 10% formaldehyde and fixed them at  $4^\circ\text{C}$  for 24 hours. To standardize the appropriate compared section from both the OA and CR TKA groups, an area in the distal third of the ligament 100  $\mu\text{m}$  above the joint line was isolated. The specimens were then embedded in paraffin and the distal and proximal aspects marked to assure the same areas of each PLC were being compared.

We then sectioned the PCL specimens to a thickness of 8  $\mu\text{m}$  in two transverse planes and identified 100  $\mu\text{m}$  from the tibial joint line and the two sections were 100  $\mu\text{m}$  apart. These two sections were then mounted on lysine-coated microscope slides. The two sections spaced 100  $\mu\text{m}$  apart from the distal third of the ligament were then stained and examined microscopically.

We used a previously reported immunohistochemistry histologic technique [14]. After blocking nonspecific binding (with 3% normal horse serum), sections were incubated overnight at 4°C in a humid chamber with commercially available mouse monoclonal antibodies against neurofilament protein (NFP) and S-100 protein (Millipore, Billerica, MA, USA). We used these to label the central axon, the periaxonic Schwann-related cells, and the perineural-related cells of the mechanoreceptors. The stock NFP was diluted at a ratio of 1:200 with blocking solution, and stock S-100 was diluted at a ratio of 1:500 with blocking solution. Blocking solution consisted of 3.3 mL phosphate-buffered saline and one drop of goat serum from a Vectastain ABC kit. The antigen-antibody reaction was developed using a commercially available kit (Vectastain ABC) with DAB as the chromagen (Vector Labs, Burlingame, CA, USA). One of us (WMM) then determined the presence and/or absence of mechanoreceptor organs at  $\times 40$  magnification under light microscopy. The classification system of Freeman and Wyke was used to determine the types of receptors that were present (Type 1: Ruffinilike; Type 2: Pacinilike; Type 3: Golgi/fusiformlike; and Type 4: free nerve ending) [8]. A quantitative analysis of the transverse sections was then undertaken for each CR TKA and OA PCL specimen and the area of stained elements recorded for comparison. We analyzed each of the transverse sections for positively stained elements using Aperio Imagescope software (Aperio Technologies Inc, Vista, CA). The strong positive elements as

defined by comparison to a control section of skin epidermis were assigned a number of pixels as determined from the control hue threshold for positive staining and were then converted to an area and the OA and TKA sections compared.

We compared the percentages of areas of positive staining in each group using a Student's *t* test (Excel, Microsoft, Corp., Redmond, WA, USA).

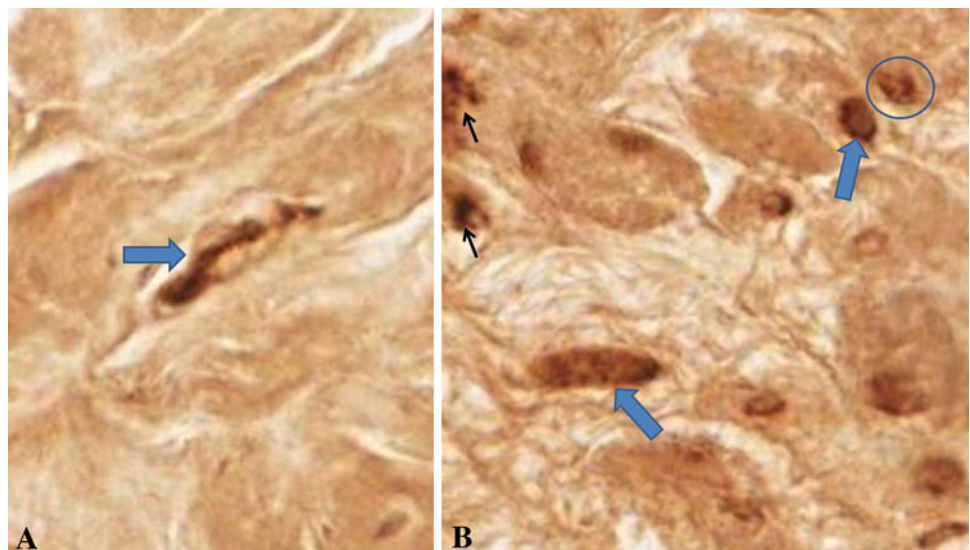
## Results

The immunohistochemical histologic investigation revealed evidence of positively stained elements with both S-100 protein and NFP immunohistochemical staining in all specimens in both groups. Morphologically, these elements appear to correspond to Type 1: Ruffinilike; Type 2: Pacinilike; and Type 3: Golgi and fusiform types of mechanoreceptors (Fig. 3). We found no difference ( $p = 0.18$  for NFP and  $p = 0.86$  for S-100 staining) in the percentage of areas for receptors in the two groups. The digitized histology of transverse sections of sampled ligament revealed that the OA specimens had an average percent area of  $10.1\% \pm 7.1\%$  (range, 4.5%–24.3%) positively stained elements for NFP staining and  $11.1\% \pm 7\%$  (range, 4.3%–26.6% per PCL) area of positively stained elements for S-100 staining. In the CR TKA PCL group, the percent area of positively stained elements was  $7.4\% \pm 4.4\%$  for NFP (range, 1.0%–10.4%) and  $10.7\% \pm 5.1\%$  for S-100 staining (range, 9%–11.8%).

## Discussion

The function of the PCL in primary TKA and whether to retain it has been a source of controversy. Although

**Fig. 3A–B** Example of a histologic section from a cruciate-retaining (CR) TKA with S-100 staining. **(A)** A Pacinilike receptor (arrow) and from a CR TKA. **(B)** S-100 staining with Ruffinilike (small arrows) and lamellarlike receptors (large arrows). A circle is around positive staining that may resemble free nerve endings.



previous studies suggest OA knees have PCL histology that is not comparable to normal knee PCLs, they have reported that these ligaments in OA contain mechanoreceptor organs [5, 20, 22]. However, it is unclear whether mechanoreceptors persist after performing a CR TKA. If they remain, then we might not look for or understand their clinical importance after a TKA. We therefore determined the presence and area of mechanoreceptors of PCLs after they have functioned in a CR TKA compared with PCLs retrieved in OA knees during primary posterior-stabilized TKA.

Our study is subject to a number of assumptions and limitations. First, we cannot determine whether these receptors are functioning normally. Reports concerning differences between patients who obtain a CR versus a posterior-stabilized type of knee found no difference in gait analysis or position sense of the knee after surgery [4, 13, 23, 24]. It is possible other receptors about the knee including within the knee capsule could be allowing patients enough position sense to make it difficult to measure a difference between the two groups. The question still exists, however, whether the PCL allows a better stability profile in flexion where the PCL reportedly gives the most support to coronal rotation and sagittal posterior-directed forces after CR TKA [14, 15, 19]. The fact that the PCL continues to retain these receptors suggests they are functioning because OA knees have fewer mechanoreceptors compared with normal knees. Therefore, if the receptors continue to be present, it may indicate that they are functioning in at least a similar manner as in the OA knee. Second, the entire ligament was not analyzed in a sequential manner. We examined two transverse sections in the distal third of the PCL in OA and CR TKA and compared them for the area of positive immunohistochemical staining for S-100 and NFP. The more distal tibial insertion location was chosen because Schutte and coworkers showed the specialized mechanoreceptors are more concentrated in this region of cruciate ligaments [21, 22]. The fact that the analyzed sections were standardized between the two groups and taken from the same transverse sectional area gives an adequate reasoning to the analysis technique used for comparison of the two groups. Third, we have no way to determine if the surgical technique used in the CR TKA specimens that were analyzed played a role in our findings. Unfortunately, we do not have this information from our retrieval program but the fact that the area of positive neural element staining was not statistically different from the OA to CR TKA group means the decrease in receptors reported in OA PCLs is not further decreased after CR TKA [7].

We found when the PCL is retained, it can maintain its mechanoreceptors compared with OA PCLs, which had similar areas of staining in the distal third of the ligament. Our observations suggest the PCL can retain its

microarchitecture when retained during TKA but without information from the surgical cases, it may be difficult to draw any conclusions as to what parameters are involved in its successful retention or how it may be functioning. The roll-forward pattern of wear on the medial side of the polyethylene inserts on several of these retrievals may suggest that the PCL did not function to create rollback, but it may have been involved in proper balancing of the knee in the coronal plane [15, 19]. However, one can argue that with the retention of mechanoreceptors, the physiology and mechanics of the knee may somehow benefit functionally by retaining the PCL during TKA. Several studies reported no benefit to PCL retention after TKA [3, 12, 23]. However, one study suggested that when the knee is balanced in flexion and extension that proprioception after TKA is improved [23]. This along with the fact that OA knees have decreased proprioception with varus deformity could imply that as long as the knee is well balanced with soft tissue gaps that are rectangular in flexion and extension, the knee will improve its proprioceptive abilities regardless of whether the PCL is present.

Although our study was not conducted to answer the question of whether the PCL should be retained after surgery, the ligament appears to maintain its mechanoreceptors after CR TKA, at least in a similar area as in the OA knee.

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