Attune®
Knee System

Evidence Summary of the ATTUNE® Knee System

The ATTUNE® Knee System evidence generation program gathers evidence from company initiated studies, investigator initiated studies, independent publications, and national joint registries. ATTUNE Knee System results are recorded in terms of implant survivorship, Patient Reported Outcome Measures (PROMs), fluoroscopic and radiostereometric analyses (RSA).

The ATTUNE Knee System results detailed below demonstrate how the ATTUNE Knee addresses challenges in total knee arthroplasty (TKA) such as crepitus, patient satisfaction, stability, survivorship, fixation, and recovery.

ADDRESSING INDUSTRY CHALLENGES

Patellofemoral Outcomes

Four peer reviewed studies have independently concluded the same result: improved patellofemoral outcomes with the ATTUNE Knee compared to the well-performing SIGMA® Knee.[1-4]

One in vivo biplanar fluoroscopy study[5] concluded the biomechanics of the PS RP ATTUNE Knee with medialized anatomic patella more closely resembles the biomechanics of the natural knee than the PS RP ATTUNE Knee medialized dome patella.[5]

Patient Satisfaction

One study, which compared the results of two worldwide, multi-center perspective studies concluded the ATTUNE Knee System has **shown statistically significant improvements** in **multiple** PROMs compared to a leading knee brand.[6]

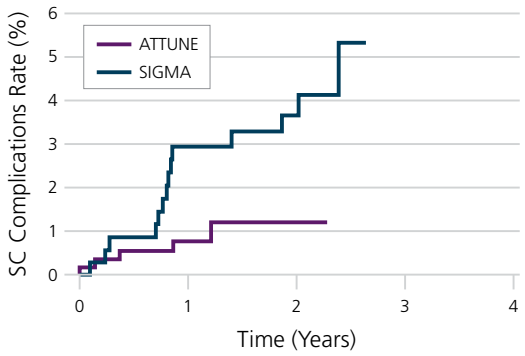


Figure 1

Cumulative Incidence Rate of Symptomatic Crepitus (SC) for ATTUNE PS Knees compared to SIGMA PS Knees. Results demonstrated a statistically significant decrease in Symptomatic Crepitus (log-rank p-value=0.017)[4]

STABILITY:

Three studies [7,13,14] examined mid-flexion stability with the ATTUNE Knee System.

During deep knee bend, level gait and ramp down, Sharma et al.[13] found the patients implanted with PS FB ATTUNE Knee *in vivo* demonstrated consistent axial rotation and posterior femoral rollback with weight bearing flexion. "Subjects experienced low overall paradoxical anterior sliding and no incidence of condylar lift off leading to mid-flexion stability."

Pfitzner et al.[14] studied *in vivo* mid-flexion stability with the CR RP ATTUNE Knee. The results of this study demonstrated increased mid flexion stability with the ATTUNE GRADIUS™ Curve compared to the traditional J Curve design that was examined in this study. This was seen by both increased lateral roll-back and the elimination of paradoxical anterior slide of the medial condyle that can be associated with the traditional J Curve design.[14]

During in vivo activities of daily living (ADL)-walking, stair descent, deep knee bend, sitting and standing from a chair, List et al.[23] found the CR FB ATTUNE Knee eliminated paradoxical anterior slide at 30 degrees flexion. Compared to the traditional J curve design of the CR FB P.F.C.™ SIGMA Curved Plus, the CR FB ATTUNE Knee demonstrated improved lateral femoral rollback above 30 degrees, during gait activities, and during tasks transitioning from standing to sitting.[23]

Takagi, et al.[7] found the CR FB ATTUNE Knee intra-operative *in vivo* kinematics replicated the stability predicted *in vitro* and **demonstrated better kinematic performance** in Japanese women compared to the other TKA examined in this study. It is worth noting that approximately 82% of knee arthroplasty patients in Japan were female.[15]

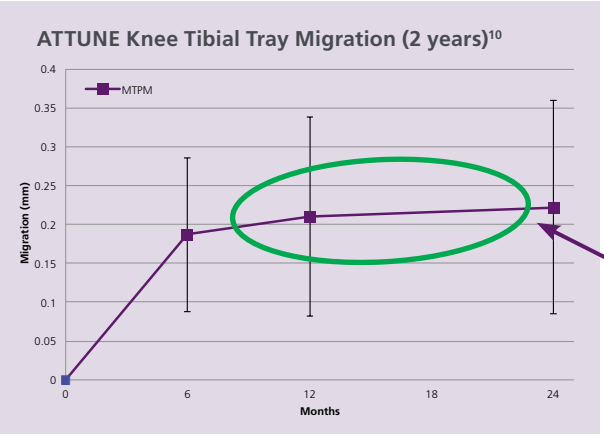
Smooth roll-back movement without abrupt change at mid-flexion was observed in patients receiving the ATTUNE Knee System.[7,13,14,23]

RSA (RADIOSTEREOMETRIC ANALYSIS): A PREDICTIVE LONG-TERM SURVIVORSHIP MEASURE

- RSA is an imaging technology used to precisely measure implant migration.
- Two key publications[11,12] have established criteria to interpret RSA results; which allows early two-year follow-up RSA measurements to help predict long term survivorship (Figure 2).
- Two studies have measured RSA results with the ATTUNE Knee:
  - Richardson et al.[10] found ATTUNE Knee Tibial Base migration of 0.21 mm at two years. This minimal migration is encouraging.
  - Kaptein et al.[16] found no difference in mean maximum total point motion (MTPM) for both tibial bases (Figure 3a) and femoral components (Figure 3b) between the ATTUNE Knee and P.F.C. SIGMA Knee in a prospective, randomized controlled trial followed for two years.

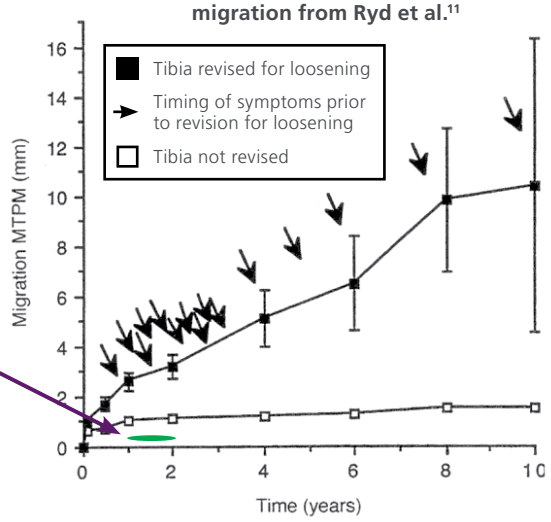
The image on the left shows ATTUNE Knee tibial base component migration at 2 years of 0.21 mm.[10] Comparing the ATTUNE Knee's performance from the graph of Richardson et al.[10] (ATTUNE Knee, on the left) with the graph from Ryd et. al.[11] (Non-ATTUNE Knee, on the right), the **ATTUNE Tibial Base has low migration**, which has been shown to be predictive of no early revisions due to aseptic loosening.[11,12]

Figure 2



ATTUNE Knee results from Richardson et al.[10] overlaid on published criteria from Ryd et al.[11] indicating no early revisions due to aseptic loosening

Diagram representing tibial component migration from Ryd et al.[11]



Graph shows migration of 143 tibial components studied. ATTUNE Knee data overlaid (green oval) for interpretation purposes.

Figure 3a: Migration Tibia[16]

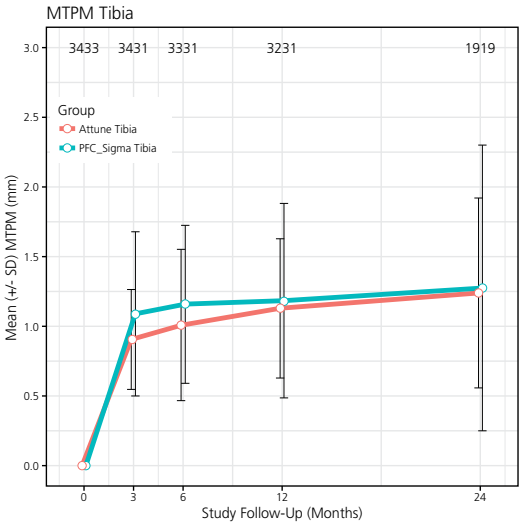
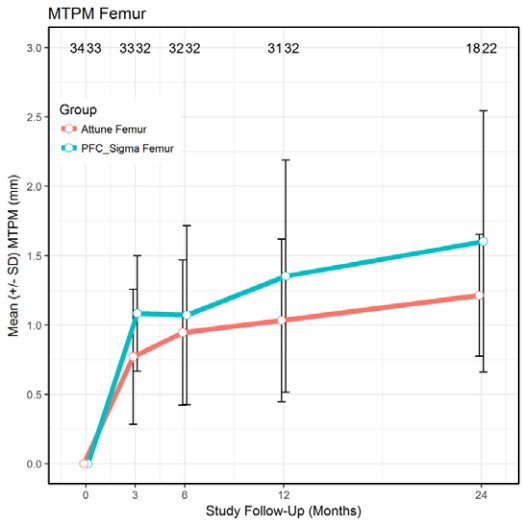


Figure 3b: Migration Femur[16]



The image to the far left (Figure 3a) demonstrates the ATTUNE Knee Tibial Base has no statistically significant difference in the MTPM compared to the P.F.C. SIGMA Knee Tibial Base which, mentioned previously, has been shown to be predictive of no early revisions due to aseptic loosening.[11,12] Also, lower variation in MTPM (significant) than the P.F.C. SIGMA Knee Tibial Base (Levene's test) was observed.[16]

Femoral components results from the same study are shown in the image to left (Figure 3b) and demonstrate similar findings as the tibial analysis: there was no statistically significant difference in the MTPM of the ATTUNE Knee vs SIGMA Knee Femoral Components.[16]

REGISTRY RESULTS:

The ATTUNE Knee appears to be performing in line with the class of TKA as demonstrated by current results from a number of joint registries.[8,9,17,18,21,22]

The Implant Summary Report dated February 14th, 2019 obtained by DePuy Synthes from the National Joint Registry for England, Wales, Northern Ireland, and the Isle of Man (NJR) provides an independent analysis of 23,321 ATTUNE Knee implantations. This analysis showed that the cumulative revision rate (CRR) for the ATTUNE Knee is 2.8% (95% CI: 2.1, 3.5%) at five years (97.2% implant survivorship at five years), which is in line with the overall class of total knee replacement of 2.2% CRR (2.2, 2.2%) at five years.[8] The 6 year estimated cumulative rate of revision for the ATTUNE Knee is currently based on a sample size of 83 patients.[8]

NJR IMPLANT SUMMARY REPORT

97.2% – Implant Survivorship at five years[8]

The Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) publishes an annual report with outcomes data at set intervals of one, three, five-year and beyond. Additional implant survivorship data is now also available more frequently to manufacturers who subscribe to the AOANJRR's Automated Industry Report System (AIRS). The AIRS reports were generated for Cruciate Retaining (CR) and Posterior Stabilized (PS) cohorts to be consistent with how the AOANJRR presents primary Total Knee Arthroplasty (TKA) results in their published annual report.

The CR report indicates that the 11,735 cemented CR ATTUNE Knees cumulative percent revision of 2.0% (95% CI: 1.6, 2.3%) at four years is performing significantly better than all other TKA in the AOANJRR (HR 0.65 (0.48, 0.87), p=0.003).[21]

The PS report indicates that the 5,263 cemented PS ATTUNE Knees with a cumulative percent revision of 1.8% (95% CI: 1.4, 2.4%) at four years is performing significantly better than all other TKA in the AOANJRR (HR 0.61 (0.48, 0.78), p<0.001).[22]

All other TKA in these reports had a four year estimated cumulative percent revision of 3.1% (3.1, 3.2). The five year cumulative percent revision estimates for the CR ATTUNE Knee and PS ATTUNE Knee are based on a sample size of 78 and 143 patients, respectively.[21,22]

AOANJRR

98.0% – ATTUNE CR Knee implant survivorship at four years.[21]

98.2% – ATTUNE PS Knee implant survivorship at four years.[22]

The Michigan Arthroplasty Registry Collaborative Quality Initiative (MARCQI) is the first publicly available registry with ATTUNE Knee information from a U.S. dataset. The registry began collecting data in 2012, and captures 95% of hip and knee arthroplasties in the state. The 2018 MARCQI Report, which tracks 6,356 ATTUNE Knees, indicates implant survivorship for the ATTUNE Knee is consistent with the class of primary TKA at three years follow-up.[17]

MARCQI

97.50% – ATTUNE Knee Implant Survivorship at three years.[17]

The Kaiser Permanente Total Joint Registry, a closed total joint registry in the U.S. maintained by the Kaiser Permanente Healthcare System, began collecting data in 2001. A 2 year implant survivorship study compared the FB ATTUNE Knee (N=1,707) and FB SIGMA Knee (N=2,984), and found no statistical difference with both having greater than 98% implant survivorship at 2 years (p=0.638). None of the 1,707 FB ATTUNE Knees were revised for pain or aseptic loosening in this study.[9]

KAISER

Over 98% - ATTUNE Knee Implant Survivorship at two years[9]

Early Recovery with the ATTUNE Knee

A single surgeon, single center study compared the early postoperative outcomes for 40 patients implanted with CR RP ATTUNE Knees compared to a 40 patient cohort of CR150 RP SIGMA Knees. The results, seen in Table 1 below, showed improvements with the ATTUNE Knee in some of the early postoperative outcomes compared to the well performing SIGMA Knee.[19]

ATTUNE Knee RP patients have less pain, better motion and improved function compared to the SIGMA Knee RP patients in this short term follow up study.[19]

Table 1: Early Outcome Study of the ATTUNE Knee vs the SIGMA CR150 Knee[19]

	ATTUNE CR RP Knee N=40 knees	SIGMA CR150 RP Knee N=40 knees	Significance
2 week flexion (°)	113.0° (8.6)	106.1° (9.5)	p<0.001
6 week flexion (°)	121.1° (6.0)	115.0° (9.6)	p=0.002
Functional Score SF 1	6.6 (1.5)	5.3 (1.5)	p<0.001
Discharge pain at rest	0.4 (0.6)	0.8 (1.1)	P=0.048, trending

Numbers in parentheses denote standard deviations
A p value between 0.01 and <0.05 is noted as trending
A p value <0.01 is statistically significant

A multi-center study recorded both patient reported and surgeon reported outcomes pre-operatively, and at 6 weeks, 3 months, 6 months, 12 months, and 24 months follow-up. Compared to the pre-operative baseline, the **greatest clinical improvements** with the ATTUNE Knee occurred in the **first 6 weeks**.[20]

The interim results on 200 patients also found statistically significant improvements in KOOS-PS at 6 months (p<0.001), improvements prior to 6 months (p<0.001), and superior pain and PROMs at 6 weeks compared to pre-operative baseline.[20]

Results - Primary Objective[20]

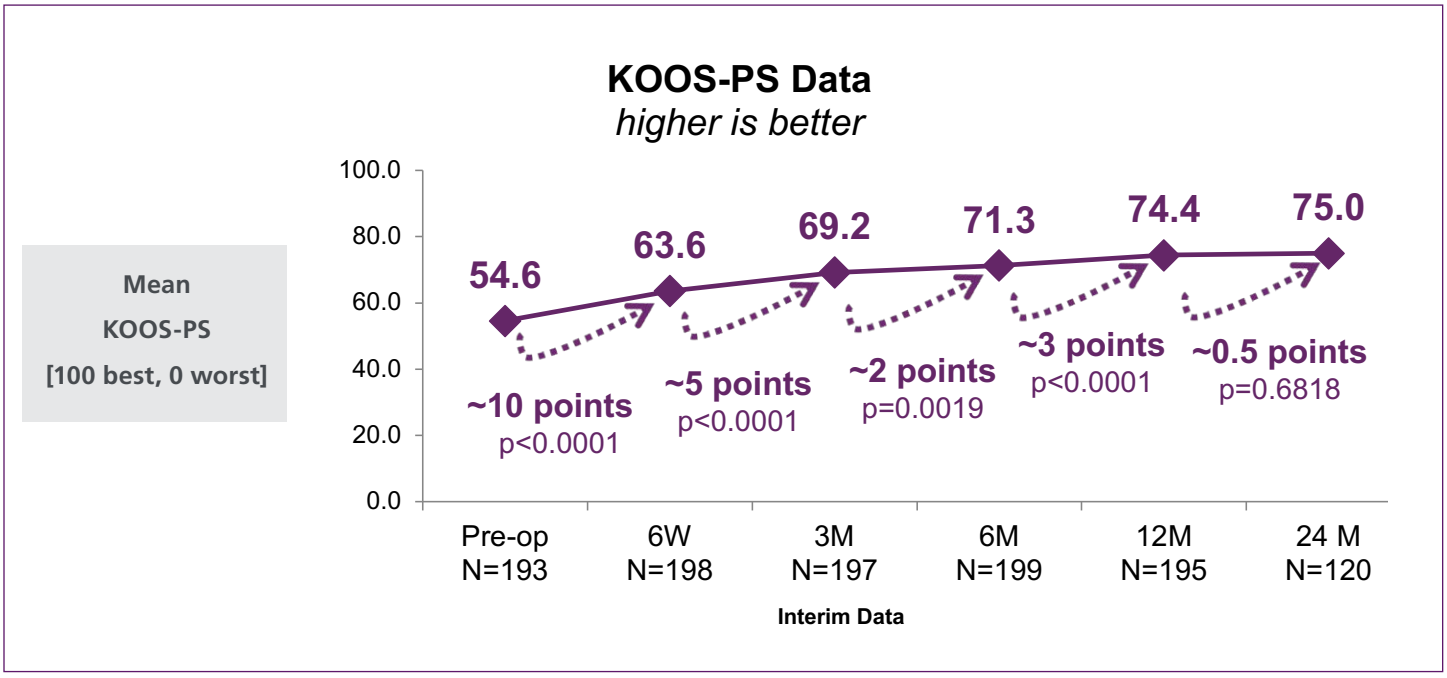


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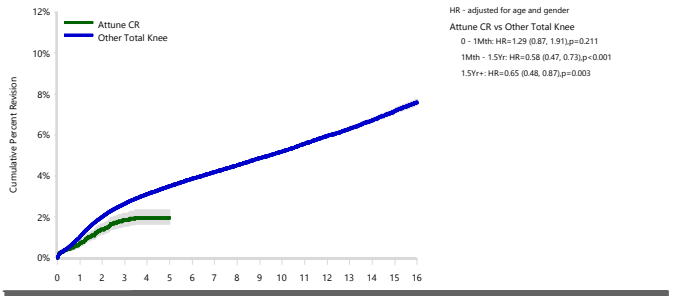
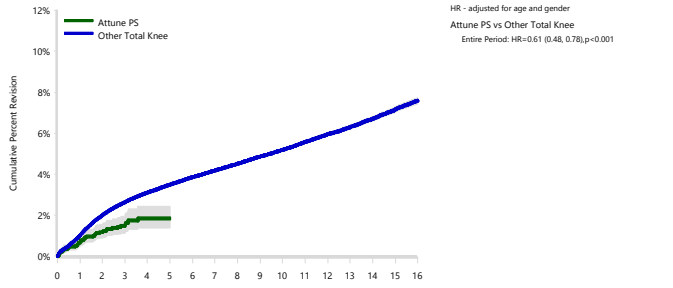
Figure 1: Cumulative Percent Revision of Primary Total Knee Replacement by Model (All Diagnoses)



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs
Attune CR	11735	8777	5562	3094	957	78	0	0
Other Total Knee	641149	583415	521276	463086	407188	354512	304806	258400

Number at Risk	8 Yrs	9 Yrs	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs
Attune CR	0	0	0	0	0	0	0	0	0
Other Total Knee	215396	176192	141949	111473	85564	63322	44295	28922	16523

Figure 1: Cumulative Percent Revision of Primary Total Knee Replacement by Model (All Diagnoses)



Number at Risk	0 Yr	1 Yr	2 Yrs	3 Yrs	4 Yrs	5 Yrs	6 Yrs	7 Yrs
Attune PS	5263	4003	2627	1588	690	143	0	0
Other Total Knee	647621	588189	524211	464592	407455	354447	304806	258400

Number at Risk	8 Yrs	9 Yrs	10 Yrs	11 Yrs	12 Yrs	13 Yrs	14 Yrs	15 Yrs	16 Yrs
Attune PS	0	0	0	0	0	0	0	0	0
Other Total Knee	215396	176192	141949	111473	85564	63322	44295	28922	16523

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