



Evidence Summary of the ATTUNE® Knee System

The ATTUNE® Knee System evidence generation program gathers evidence from company initiated studies, investigator initiated studies, 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, and fixation.

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^{5,13} concluded the biomechanics of the PS RP ATTUNE Knee with medialized anatomic patella more closely resembles the biomechanics of the natural knee than the medialized dome patella.^{5,13}

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 certain leading knee brands.⁶

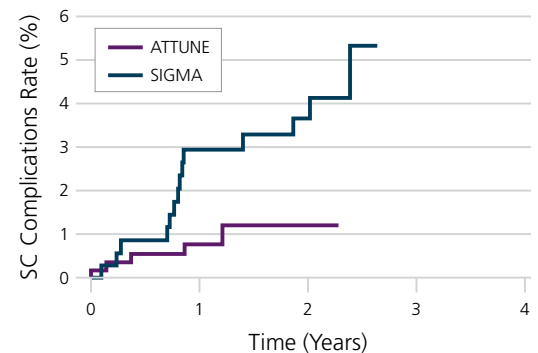


Figure 1

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:

Two studies examined mid-flexion stability with the ATTUNE Knee System.

Pfzner et al.¹⁴ studied in vivo mid-flexion stability with the CR RP ATTUNE Knee. In their study, they found roll back with no paradoxical anterior slide, when comparing the ATTUNE Knee to J-Curve designs like the SIGMA Knee.¹⁴

Tagagi, et al.⁷ found the CR FB ATTUNE Knee in vivo kinematics replicated the stability predicted in vitro and **demonstrated a more natural kinematic pattern** in Japanese women compared to the predicate TKA examined in this study. It is worth noting that approximately 82% of knee arthroplasty patients in Japan were female.¹⁵

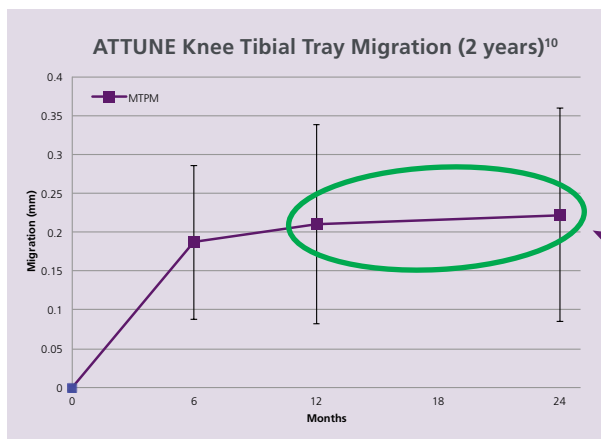
Smooth roll-back movement without abrupt change at mid-flexion was observed in patients receiving the ATTUNE Knee System.

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 MTPM between the ATTUNE Knee and P.F.C.™ SIGMA Knee (Figure 3) in a prospective, randomized controlled trial followed for two years.

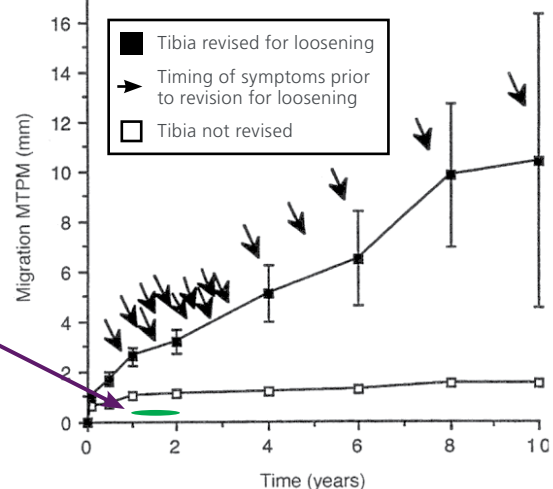
The image on the left shows ATTUNE Knee migration at 2 years of 0.21 mm.¹⁰ Comparing the ATTUNE Knee's performance from the graph of Richardson et al.¹⁰ (ATTUNE Knee, on the left) with the graph from Ryd et al.¹¹ (Non-ATTUNE Knee, on the right), the **ATTUNE Tibial Base has low migration**, which has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

Figure 2



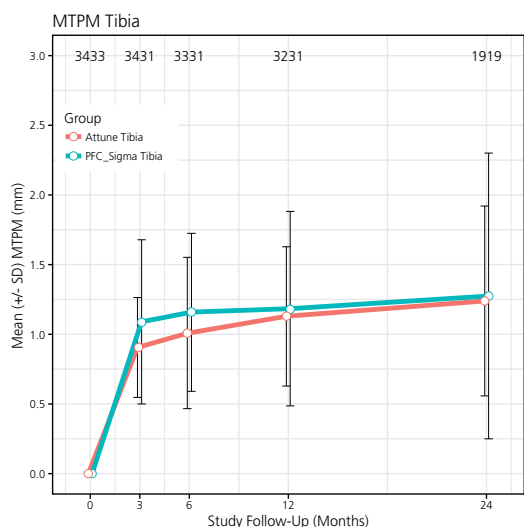
ATTUNE Knee results from Richardson et al.¹⁰ overlaid on published criteria from Ryd et al.¹¹ indicating no early revisions due to aseptic loosening

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 3: Migration Tibia¹⁶



The image to the left demonstrates the ATTUNE Knee has lower variation in MTPM (significant) than the P.F.C. SIGMA Knee (Levene's test).¹⁶ This study also found low migration with the ATTUNE Tibial Base which, mentioned previously, has been shown to be predictive of no early revisions due to aseptic loosening.^{11,12}

REGISTRY RESULTS:

The Implant Summary Report dated November 10th 2017 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 14,936 ATTUNE Knee implantations. This analysis showed that the cumulative revision rate (CRR) for the ATTUNE Knee is 1.9% at four years (98.1% implant survivorship at four years), which is in line with the overall class of total knee replacement CRR which is 1.9% at four years.⁸ The 5 year estimated cumulative rate of revision for the ATTUNE Knee is currently based on a sample size of 64 patients, with two late revisions influencing this estimate.⁸

NJR IMPLANT SUMMARY REPORT

98.1% – Survivorship at four years⁸

Per the 2017 AOANJRR report, in which 8,384 ATTUNE Knees are being tracked (N=5,691 CR, N=2,693 PS), the ATTUNE Knee estimated cumulative percent revision was 2.1% (1.4, 3.1) for ATTUNE Cruciate Retaining Knee, 1.1% (0.6, 1.9) for ATTUNE Posterior Stabilized Knee at three years.⁹ The CR ATTUNE Knee performs in line with the overall class of cemented, minimally stabilized total knee arthroplasty (TKA) at three years which has an estimated cumulative percent revision of 2.2% (2.1, 2.3).⁹ The PS ATTUNE Knee compares favorably with the overall class of posterior stabilized cemented total knee arthroplasty (TKA) at three years which has an estimated cumulative percent revision of 2.9% (2.8, 3.0).⁹ A table including selected TKR products based on the four largest device manufacturers by worldwide sales is included in the references.

AOANJRR

97.9% – ATTUNE Cruciate Retaining Knee survivorship at three years.⁹

98.9% – ATTUNE Posterior Stabilized Knee survivorship at three years.⁹

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Australian Orthopedic Association National Joint Replacement Registry 2017 Annual Report

Extracted from Table KT7 Cumulative Percent Revision of Cemented Primary Total Knee Replacement by Prosthesis Combination

Femoral Component	Tibial Component	N Revised	N Total	1 Yr	3 Yrs	5 Yrs	10 Yrs	15 Yrs	16 Yrs
Attune CR	Attune	49	5691	0.6 (0.4, 0.9)	2.1 (1.4, 3.1)				
Attune PS	Attune	18	2693	0.4 (0.2, 0.8)	1.1 (0.6, 1.9)				
Genesis II CR	Genesis II	466	13669	0.9 (0.8, 1.1)	2.4 (2.1, 2.7)	3.1 (2.8, 3.4)	4.3 (3.9, 4.7)	5.6 (4.9, 6.5)	6.0 (5.0, 7.1)
Genesis II CR	Profix Mobile*	35	490	1.7 (0.8, 3.3)	3.4 (2.1, 5.4)	5.4 (3.7, 8.0)	9.0 (6.3, 12.9)		
Genesis II Oxinium CR	Genesis II	347	7488	1.0 (0.8, 1.3)	2.8 (2.4, 3.2)	3.7 (3.2, 4.2)	6.1 (5.5, 6.9)	10.9 (8.3, 14.2)	
Genesis II Oxinium PS	Genesis II	785	15823	1.5 (1.3, 1.7)	3.8 (3.5, 4.1)	5.2 (4.8, 5.6)	7.5 (6.9, 8.1)		
Genesis II PS	Genesis II	571	15816	1.2 (1.1, 1.4)	2.8 (2.6, 3.1)	3.7 (3.4, 4.0)	5.0 (4.5, 5.5)	6.2 (5.2, 7.3)	
Nexgen CR	Nexgen	119	3853	0.6 (0.4, 0.8)	1.4 (1.1, 1.9)	1.9 (1.5, 2.4)	2.9 (2.4, 3.6)	5.1 (4.0, 6.4)	5.1 (4.0, 6.4)
Nexgen CR Flex	Natural Knee II	8	804	0.2 (0.1, 1.0)	0.7 (0.3, 1.8)	0.7 (0.3, 1.8)			
Nexgen CR Flex	Nexgen	315	19517	0.7 (0.6, 0.8)	1.5 (1.3, 1.7)	2.1 (1.8, 2.3)	2.8 (2.4, 3.2)		
Nexgen LCCK	Nexgen	29	706	2.0 (1.1, 3.4)	3.6 (2.4, 5.5)	5.2 (3.5, 7.7)	5.2 (3.5, 7.7)		
Nexgen LPS	Nexgen	239	5776	1.0 (0.8, 1.3)	2.3 (2.0, 2.8)	3.0 (2.5, 3.5)	4.8 (4.2, 5.5)	6.0 (5.2, 7.0)	6.0 (5.2, 7.0)
Nexgen LPS Flex	Nexgen	956	29701	0.9 (0.8, 1.0)	2.3 (2.1, 2.5)	3.1 (2.9, 3.4)	5.0 (4.7, 5.4)		
PFC Sigma CR	MBT	28	1153	0.9 (0.5, 1.6)	1.7 (1.1, 2.6)	2.1 (1.4, 3.2)	3.0 (2.0, 4.3)		
PFC Sigma CR	PFC Sigma	318	12226	0.8 (0.7, 1.0)	2.0 (1.7, 2.2)	2.4 (2.1, 2.7)	3.4 (3.0, 3.9)	5.7 (4.6, 7.1)	
PFC Sigma PS	MBT	231	5971	0.9 (0.7, 1.2)	2.7 (2.3, 3.1)	3.5 (3.0, 4.0)	4.8 (4.2, 5.5)		
PFC Sigma PS	PFC Sigma	274	7600	1.2 (0.9, 1.4)	2.5 (2.2, 2.9)	3.2 (2.8, 3.6)	4.7 (4.1, 5.4)	7.2 (5.9, 8.8)	
Persona	Persona	6	821	0.5 (0.2, 1.5)	1.5 (0.6, 3.5)				
Triathlon CR	Triathlon	607	31060	0.8 (0.7, 0.9)	2.0 (1.8, 2.2)	2.5 (2.3, 2.7)	3.9 (3.4, 4.5)		
Triathlon PS	Triathlon	219	6676	1.4 (1.2, 1.7)	3.1 (2.6, 3.6)	4.0 (3.4, 4.5)	5.1 (4.3, 6.0)		
Vanguard CR	Maxim	178	7915	0.6 (0.5, 0.8)	2.2 (1.9, 2.7)	2.9 (2.5, 3.4)	4.3 (3.5, 5.3)		
Vanguard CR	Vanguard	16	983	0.5 (0.2, 1.2)	1.2 (0.7, 2.2)	1.4 (0.8, 2.6)			
Vanguard PS	Maxim	193	3751	1.9 (1.5, 2.4)	4.5 (3.8, 5.3)	5.7 (4.9, 6.6)	7.5 (6.1, 9.3)		

Table KT22 Cumulative Percent Revision of Minimally Stabilised Primary Total Knee Replacement by Fixation (Primary Diagnosis OA)

Fixation	N Revised	N Total	1 Yr	3 Yrs	5 Yrs	10 Yrs	15 Yrs	16 Yrs
Cemented	4712	157680	0.8 (0.8, 0.9)	2.2 (2.1, 2.3)	2.9 (2.9, 3.0)	4.5 (4.3, 4.6)	6.5 (6.2, 6.9)	6.9 (6.5, 7.3)
Cementless	4795	102625	1.2 (1.1, 1.2)	3.2 (3.0, 3.3)	4.2 (4.1, 4.4)	6.1 (5.9, 6.3)	8.5 (8.1, 8.9)	9.6 (8.9, 10.3)
Hybrid	3804	118721	0.8 (0.8, 0.9)	2.3 (2.2, 2.4)	3.1 (3.0, 3.2)	4.6 (4.4, 4.7)	6.4 (6.1, 6.7)	7.0 (6.4, 7.6)
TOTAL	13311	379026						

Note: Excluding cementless Genesis Oxinium and Profix Oxinium femoral prostheses

Table KT23 Cumulative Percent Revision of Posterior Stabilised Primary Total Knee Replacement by Fixation (Primary Diagnosis OA)

Fixation	N Revised	N Total	1 Yr	3 Yrs	5 Yrs	10 Yrs	15 Yrs	16 Yrs
Cemented	4774	124375	1.1 (1.1, 1.2)	2.9 (2.8, 3.0)	3.9 (3.8, 4.1)	5.9 (5.8, 6.1)	7.8 (7.3, 8.3)	8.0 (7.3, 8.8)
Cementless	337	6947	1.9 (1.6, 2.2)	4.0 (3.5, 4.5)	5.0 (4.5, 5.6)	6.3 (5.6, 7.1)		
Hybrid	675	11458	1.6 (1.4, 1.8)	4.2 (3.8, 4.6)	5.5 (5.1, 6.0)	7.3 (6.7, 7.9)	10.3 (9.0, 11.8)	10.9 (9.3, 12.8)
TOTAL	5786	142780						

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