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Prodromidis, AD, Chloros, GD, Thivaivos, GC et al. (2023) High rate of radiolucent lines following the cemented original design of the Attune total knee arthroplasty: a systematic review and meta-analysis. *Bone and Joint Journal*, 105-B (6). pp. 610-621. ISSN: 2049-4394

<https://doi.org/10.1302/0301-620X.105B6.BJJ-2022-0675.R1>

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1 **High rate of radiolucent lines following the cemented original design of the ATTUNE®**
2 **total knee arthroplasty. A systematic review and meta-analysis**

3
4 **Aims:** Component loosening can be associated with the development of radiolucent lines
5 (RLLs). Our study aimed to assess the RLL rate in the cemented original version of the
6 ATTUNE® TKA and their relationship to loosening.

7 **Materials and Methods:** A systematic search was undertaken using the Cochrane
8 methodology in four online databases. Studies were screened against predetermined criteria,
9 and data were extracted. Available National Joint Registries in the Network of Orthopaedic
10 Registries of Europe were also screened. Random effects model meta-analysis was conducted.

11 **Results:** Twelve of 263 studies (n=3,869) were included. Meta-analysis of 10 studies showed
12 high rates of overall tibial or femoral RLLs for the cemented original version of the ATTUNE®
13 TKA. The rate of any RLL was estimated at 21.4% (95%CI: 12.7-33.7%) for all implant types
14 but was higher for certain subgroups: 27.4% (95%CI: 13.4-47.9%) for the CR type, and 29.9%
15 (95%CI: 15.6-49.6%) for the fixed-bearing type. Meta-analysis of 5 studies comparing the
16 ATTUNE with other implants showed a higher risk of overall tibial or femoral RLLs (OR:
17 2.841; 95%CI: 1.219-6.623, P=0.016) in the ATTUNE. Component loosening or revision for
18 loosening as reported by research studies were lower, estimated at 1.2% and 0.9% respectively,
19 but reported rates varied from 0 to 16.3%. The registry data examined did not report specifically
20 on the original ATTUNE® TKA or on revision due to loosening, but “all-cause” 5-year
21 revision rates varied from 2.6 to 5.9% at 5 years between registries.

22 **Conclusion:** The original cemented ATTUNE® TKA system is associated with high rates of
23 RLLs, but their clinical significance is uncertain given the overall low reported rates of
24 component loosening and revision. However, in view of the observed high RLL rates and the
25 observed variation in the rates of component loosening and revision between studies and
26 registries, close surveillance of the original ATTUNE® system is recommended.

27
28 **TAKE HOME MESSAGE**

- 29 • The original ATTUNE® TKA system is associated with a high rate of radiolucencies.
30 • The mechanism accounting for these radiolucencies is uncertain, hence it cannot be
31 concluded if modifications of the tibial tray under surface will address these issues.
32 • Close surveillance of the original design of the ATTUNE TKAs is recommended.

33 **INTRODUCTION**

34

35 The ATTUNE® (DePuy Synthes, Warsaw, IN, USA) was the successor to the PFC Sigma,
36 (DePuy Orthopaedics Inc., Warsaw, IN, USA) in part due to reported anterior knee problems
37 and dissatisfaction rates up to 21%^{43,50}. The ATTUNE® knee prosthesis was introduced in a
38 limited launch in 2011 and in general sale in 2013²¹. In 2014 a rotating platform type implant
39 was added⁵². The ATTUNE® was marketed as having a novel patella tracking system designed
40 to optimize patella tracking while maintaining bone coverage. This new design had a gradually
41 reduced femoral radius, enhancing the conformity between the femoral component and the
42 polyethylene (PE) insert to allow gradual femoral rollback and greater mid-flexion stability²⁰,
43³³. There was also a change from a tibial base peripheral locking design to a patented central
44 locking system aiming to provide a more constraint fixation and reduce backside micromotion
45¹⁶. The original ATTUNE tibial tray had less extensive grooves (cement pockets) in its under
46 surface³⁸.

47

48 Since its release, there have been reports of higher-than-expected rates of tibial loosening with
49 the ATTUNE® system. The first of these reporting early tibial loosening at the implant-cement
50 interface for the ATTUNE® TKA was in 2017 with 15 cases requiring revision within 2 years
51 from surgery¹². As this study did not define the population from which those revisions arose,
52 the revision rate for loosening could not be determined.

53

54 Progressive radiolucency at the implant-cement interface may be an early indicator for
55 loosening⁶³. The primary aim of this study was to assess the reported rates of radiolucent lines
56 (RLLs) following the cemented original version of the ATTUNE® TKA and compare these to
57 those of other established systems. Secondary aims were to determine if these RLLs are
58 progressive and examine the relationship between RLL rates and loosening as reported by
59 research studies and national joint registries.

60

61 **MATERIALS AND METHODS**

62

63 The Cochrane methodology for systematic reviews was followed³¹. The predefined protocol
64 was published in PROSPERO (CRD42021277816). The systematic literature search strategy
65 included searching of electronic databases and scrutinizing the references of included studies.
66 The following databases were searched in November 2022 for any studies published since

67 2012: MEDLINE (Interface: EBSCOhost); Embase (Interface: OvidSP); and CINAHL
68 (Interface: EBSCOhost). Only studies available in English were included. The search algorithm
69 comprised of 2 searches: (i) "(ATTUNE OR total knee OR TKA OR TKR") AND
70 ("radiolucen* OR loosen*") (ii) ATTUNE AND knee. Results from both searches were
71 combined and screened for studies eligible for inclusion. All available national and regional
72 joint registries in and outside Europe were identified through the Network of Orthopaedic
73 Registries of Europe ⁴, and were screened for reported loosening and revision rates for the
74 cemented ATTUNE® TKA.

75

76 Inclusion/Exclusion criteria

77 *Population/Intervention/comparators:* The intervention was primary cemented ATTUNE®
78 TKA.

79 *Outcomes:* Primary outcomes were the reported presence of RLLs at the implant-cement
80 interface on AP and/or lateral follow-up postoperative radiographs. Radiolucency was defined
81 as any RLL at the implant-cement interface on AP and/or lateral standing radiographs ²³.
82 Secondary outcomes were: (i) whether RLLs were progressive and (ii) loosening rates and
83 revision rates due to loosening assessed from research clinical studies and national joint
84 registries.

85 *Study designs:* Randomized controlled studies, prospective and retrospective cohort studies,
86 case-control studies, and case series with at least 20 patients were included. The study
87 methodology was classified according to Mathes and Pieper (2017) ⁴².

88 Two reviewers (ADP, GDC) screened independently titles and abstracts. Duplicates were
89 removed and full texts of studies considered eligible were reviewed independently. Any
90 disagreements for inclusion were discussed between reviewers and, if unresolved, with the
91 senior experienced author.

92

93 Data extraction

94 Two reviewers extracted relevant data about demographics, type of implants used, cement type,
95 definition of RLLs and radiographic evaluation system. Data about loosening and revision due
96 to loosening were also extracted as reported from included studies and from National Joint
97 Registries. Numbers reported for each group (n) in the analysis refer to numbers of TKAs rather
98 than number of patients.

99

100 Data analysis – Statistical analysis

101 The rate of RLLs reported post-operatively was the primary outcome. The rates of aseptic
102 loosening and rates of revision due to loosening (as reported by research studies and national
103 joint registries) were the secondary outcomes. For each study, post-operative RLLs, loosening
104 rates and revision rates were reported as absolute numbers and rates. Any statistically
105 significant difference between groups of comparison was calculated and reported ($p < 0.05$).
106 Risk ratios and 95% confidence intervals (CIs) were calculated for both primary and secondary
107 outcomes and combined in a random-effects model meta-analysis²². Heterogeneity was
108 assessed using τ^2 , I^2 , Q and P values. Data were analysed with Comprehensive Meta-analysis
109 version 2 (Biostat).

110

111 Assessment of methodological quality of studies and quality of evidence

112 The Cochrane Risk of Bias Tool for randomised controlled trials (RCTs)³⁰, Newcastle-Ottawa
113 scale (NOS) for prospective cohort studies⁶⁴, and the revised and validated version of
114 Methodological Index for Non-Randomised Studies (MINORS) for the retrospective
115 comparative studies⁵⁸ were used. Grading of Recommendations, Assessment, Development,
116 and Evaluation (GRADE) approach was used to assess the quality of evidence of the review²⁷.

117 **RESULTS**

118 Findings of the database searches

119 4,910 records were identified by title, 12 of which met the inclusion criteria^{8, 26, 32, 36, 37, 40, 51,}
120 ^{57, 59-62}. **Figure 1** shows the Preferred Reporting Items for Systematic reviews and meta-
121 analyses (PRISMA) flow diagram⁴⁶.

122

123 Characteristics of included studies

124 **Table 1** summarises the characteristics of included studies^{8, 26, 32, 36, 37, 40, 51, 57, 59-62}. The total
125 number of TKAs included was 3,869 (2,600 ATTUNE TKAs, 1,269 other systems). Five
126 studies that had a control group for comparison had no significant difference of age, gender,
127 and BMI between groups^{8, 36, 37, 51, 60}. The mean age of patients having an ATTUNE TKA was
128 69.6 years with 894 males and 1,636 females. All studies used the original design of the
129 cemented ATTUNE TKA system. One study did not specify the use of only the ATTUNE's
130 original version but as it was used in their institution past their patient inclusion period, that
131 series was considered to be of the original version⁵⁹. All studies reported on post-operative
132 RLLs either on tibia and/or femur. Most studies reported a mean follow-up of about 2 years,
133 but with variation in their range of follow-up from 3 months to 5.4 years; this didn't allow
134 subgroup analysis according to length of follow-up (**Table 1**).

135

136 Radiographic outcomes: Radiolucent lines

137 The definition of RLLs and the radiographic evaluation system utilised are shown in **Table 2**.
138 The systems used were the Knee Society Radiographic Evaluation System and Methodology
139 (KSRESM) (**Figure 2a**)²³, and the Modern Knee Society Radiographic Evaluation System and
140 Methodology (MKSRESM) (**Figure 2b**)⁴⁴. One study defined as radiolucency any medial
141 tibial bone resorption on AP and lateral radiographs and classified it using a novel classification
142 system. Data from this referring to RLLs at the implant cement interface were extracted⁵⁹.

143

144 Results are summarised in **Table 3**. Four studies with a control group showed higher rates of
145 RLLs, predominantly tibial or overall, for the ATTUNE groups^{8, 36, 37, 60}; with two
146 demonstrating a significant difference^{37, 60}. Two studies reported no RLL for the ATTUNE
147 group in either the tibia or femur (mean follow-up 2 years)^{51, 62}. Three studies reported on
148 progression of RLLs^{36, 37, 57}, with two studies showing no progression of the reported RLLs^{36,}
149 ⁵⁷. One reported that medial tibia RLLs were progressive: increasing from 17% for the
150 ATTUNE group at 2 weeks follow-up to 42% at 2 years follow-up³⁷. One study compared
151 patients in the ATTUNE group that had RLLs with those without RLLs³². BMI was associated
152 with increased rates of RLLs (p=0.003), with an increase of one unit of BMI increasing the
153 odds of RLL by 8%. There was no difference in implant constraint (p=0.818), cement type
154 (p=0.340), patella resurfacing (p=0.286), age (p=0.984), and sex (p=0.376) between those with
155 and without RLLs.

156

157 **Meta-analysis**

158

159 Prevalence of RLL in the ATTUNE® groups (**Table 4**)

160 All studies, (1,858 ATTUNE® TKAs), examined the prevalence of RLLs either tibial, femoral
161 or overall (any tibial or femoral), with 3 studies reporting on RLL if ≥ 2 mm or progressive^{8,}
162 ^{36, 62}. Meta-analysis of 10 studies (n=1,558) showed a prevalence of 21.4%% (95%CI: 12.7-
163 33.7%) for any RLL (tibial or femoral) overall^{8, 26, 32, 36, 37, 40, 51, 57, 60, 62}.

164

165 RLLs - Sub-group analysis (CR, PS, Fixed-bearing implants) (**Table 4**)

166 There was heterogeneity in the characteristics of the ATTUNE TKA implant types, such as
167 CR/PS, fixed/mobile bearing, patella resurfaced/not and type of cement used. Meta-analysis
168 showed a prevalence of 27.4% (95%CI: 13.4-47.9%) for any RLL (tibial or femoral) overall

169 for the CR type (either fixed or mobile-bearing) ^{8, 37, 57}, and 29.9% (95%CI: 15.6-49.6%) for
170 the fixed-bearing type (either CR or PS) ^{26, 32, 36, 37, 40, 57}. The rest of the meta-analysis results
171 are summarised in **Table 4**.

172
173 Meta-analysis was also performed to compare the reported tibial versus femoral RLLs. Meta-
174 analysis of 4 studies (n=636) reporting on both tibial and femoral RLLs showed no significant
175 difference between rates of tibial and femoral RLLs in the ATTUNE group (estimated OR:
176 0.845; 95%CI: 0.461-1.548, P=0.586; heterogeneity: tau²=0.183, I²=56.084, Q=6.831,
177 P=0.077) ^{8, 26, 36, 60}.

178
179 RLLs - Comparison with control group

180 Meta-analysis (6 studies) compared RLLs of the ATTUNE® TKA with a variety of other
181 systems (PFC Sigma®, Vanguard®, PERSONA®, LCS®) ^{8, 36, 37, 57, 60}. One study (n=200)
182 reported no RLL in either group ⁵¹. In meta-analysis methodology, studies with zero events are
183 discarded, hence this study was excluded. Meta-analysis of the remaining 5 studies (1,228
184 TKAs) showed a significantly higher rate of any RLL (tibial or femoral) overall (estimated OR:
185 2.841; 95%CI: 1.219-6.623, P=0.016; heterogeneity: tau²=0.705, I²=80.805, Q=20.838,
186 P<0.001, **Figure 3**) in the ATTUNE group as compared to the control. When excluding two
187 studies reporting only on RLLs ≥ 2mm ^{8, 36}, the odds ratio was even higher (estimated OR:
188 4.258; 95%CI: 1.271-14.261, P=0.019). Meta-analysis of 2 studies (n= 603 TKAs) comparing
189 the ATTUNE® with the PFC Sigma® showed a significantly higher rate of any RLL (tibial or
190 femoral) overall in the ATTUNE group as compared to the PFC group (estimated OR: 7.039;
191 95%CI: 4.298-11.526, P<0.001; heterogeneity: tau²=0.001, I²=0.001, Q=0.298, P=0.585) ^{37, 60}.

192
193 Loosening rates (Table 5)

194 Studies reporting on loosening rates of the ATTUNE TKA and their demographics are shown
195 in **Table 5**. It is of note that there was substantial variation in the loosening rates reported
196 between studies, varying from 0-16.3%. Meta-analysis of 6 studies showed an overall reported
197 loosening rate of 1.2% (95%CI: 0.2-6.3%) (heterogeneity: tau²=6.092, I²=93.273, Q=29.731,
198 P<0.001) ^{26, 36, 40, 57, 60, 61}. Meta-analysis of 3 studies reporting on loosening rates with fixed-
199 bearing components showed an overall reported loosening rate of 2.4% (95%CI: 0.2-25.5%)
200 (heterogeneity: tau²=4.605, I²=91.283, Q=22.942, P<0.001) ^{26, 40, 57}. Meta-analysis of 3 studies
201 reporting on loosening rates with PS components showed a rate of 1.5% (95%CI: 0.1-22.6%)
202 (heterogeneity: tau²=3.936, I²=93.702, Q=79.394, P<0.001) ^{26, 40, 59}.

203

204 **Revision due to loosening (Table 5)**

205 There was substantial variation between studies in the reported revision due to loosening rates,
206 from 0-16.3% (Table 5). Meta-analysis of 6 studies reporting on revision due to loosening
207 showed an overall rate of 0.9% (95%CI: 0.2-5.1%) (heterogeneity: $\tau^2=3.587$, $I^2=93.131$,
208 $Q=72.789$, $P<0.001$)^{26, 40, 59-62}.

209

210 Seven national joint registries reporting on the ATTUNE® knee were identified and their
211 recent reports were assessed for revision rates due to loosening (UK, Australia, New Zealand,
212 Swedish, German, Dutch, Swiss)^{1-3, 5, 48, 53, 54}. The reported revision rates are shown in Table
213 6. The registry data examined do not report specifically on the original version of the ATTUNE
214 or on revision due to loosening, but “all-cause” 5-year revision rates for the cemented
215 ATTUNE varied from 2.6 to 5.9% between registries^{2, 6, 48}, whilst for all fixation types reported
216 rates varied from 1.37 to 6.3%^{6, 48}.

217

218 **Assessment of methodological quality of the studies and quality of evidence**

219

220 The RCT had “low risk of bias”³⁰, having adequate sequence generated, concealed allocation
221 and blinding of participants without any other source of bias³⁷. Both prospective studies scored
222 the highest score of 9 stars in the assessment (Table 7). The average MINORS score of the 9
223 retrospective studies was 17 (Table 8). The quality of evidence (GRADE approach) was “low”
224²⁷.

225

226 **DISCUSSION**

227

228 Our meta-analysis showed high rates of overall tibial or femoral RLLs for the cemented
229 original version of the ATTUNE TKA. The rate of RLLs was estimated at 21.4% for all implant
230 types but was even higher for certain subgroups (27.4% for the CR type, and 29.9% for the
231 fixed-bearing type). Analysis of studies comparing RLLs of the ATTUNE versus other knee
232 systems showed that the odds of having RLL was 2.8-fold higher with the ATTUNE when any
233 RLL was considered or 4.3-fold higher when RLLs ≥ 2 mm were considered. Comparison of
234 the ATTUNE® with the PFC Sigma® showed that the odds of having RLL was 7-fold higher
235 with the ATTUNE. Rates of component loosening or revision for loosening reported within
236 published studies were much lower. Overall, these rates are estimated at 1.2% and 0.9%

237 respectively, however, reported rates varied significantly (0 to 16.3%) between studies.
238 Although, the registry data examined did not report specifically on revision of the original
239 version of the ATTUNE or on revision due to loosening, in most registries overall revision
240 rates are also low.

241

242 RLLs in TKA may be related to multiple mechanisms⁷. Early radiolucency has been attributed
243 to component design and constraint, malalignment, surface roughness of the tibial component,
244 cement type, and cementation techniques^{39, 56}. Late radiolucency around a cemented tibial
245 component has been associated with PE wear and osteolysis or stress shielding related to the
246 component material and design^{24, 25, 41}. Stress shielding is influenced by the tibial tray material
247 and thickness as well as stem length and geometry^{24, 41, 55}. Patient factors, such as age, BMI or
248 activity level, have also been linked to tibial component radiolucency^{9, 56}.

249

250 Several mechanisms have been postulated to explain the high rate of RLLs noted in the
251 ATTUNE®. A retrieval analysis examining ATTUNE implants compared with titanium PFC
252 Sigma and CoCr PFC Sigma showed no evidence of cement remain on any of the ATTUNE
253 trays¹⁷. This was felt possibly related to tibial tray design, in particular the absence of separate
254 cement pockets/grooves in the backside surface as well as the higher stem surface roughness
255 in the ATTUNE. The ATTUNE® tibial tray also has a patented central locking mechanism
256 claiming to provide more secure fixation with less backside micromotion¹⁶. However, a
257 comparative retrieval analysis showed that TKA designs with central locking trays had
258 significant less cement cover compared with peripheral locking trays; the PE inserts in the
259 central locking systems had a characteristic pattern of deformation of their outer edges, which
260 could increase the localized frictional torque and lead to debonding of the tray from the cement
261 mantle¹¹. A further possibility is that the different design and instrumentation of the ATTUNE
262 system leads to inadequate cement mantle in comparison with its predecessors, with recent
263 reports showing that excessive press fit may lead to incomplete seating or tilting of the tibial
264 component especially in hard and uneven sclerotic bone³⁵. Another factor attributed to tibial
265 loosening is stress shielding. The ATTUNE system uses a thick CoCr tibial baseplate and there
266 are reported series suggesting that medial tibial bone resorption is common with the ATTUNE,
267 presenting in various locations and severities around the baseplate⁵⁹.

268

269 Cement debonding at the tibial cement-implant interface has been related to cement type and
270 cementation technique in modern TKA^{7, 19, 45, 39}. High-viscosity (H-V) cement reaches the

271 dough phase more quickly and it is popular in TKA, however, there are reports linking H-V
272 cement with possible debonding at the implant-cement interface ^{7, 14, 39}. In our review, a
273 standard H-V cement (Palacos R+G, Heraeus Medical, Germany) was used in six of the studies
274 ^{8, 26, 32, 37, 57, 60}, with one study using a fast-setting H-V cement in some TKAs (CMW-1, DePuy,
275 CMW, UK) ³².

276

277 In 2017 DePuy launched a modification of the tibial component (Attune S+) incorporating
278 backside grooves which may facilitate cement interdigitation and improve fixation
279 performance ³⁴, but an estimated 600,000 TKAs were implanted before this design change ¹⁶.
280 Furthermore, the rest of the design features remained the same and there is, yet, little clinical
281 evidence that these changes have influenced the rates of RLL.

282

283 Radiolucencies are recognised following most cemented TKA designs and 3 studies in our
284 analysis have compared the ATTUNE® and PFC Sigma® systems with regards to RLLs ^{37, 51,}
285 ⁶⁰. Two of them showed a significantly higher rate of RLLs (both overall and especially at the
286 medial tibia implant-cement interface) in the ATTUNE as compared to the PFC ($p < 0.001$) ^{37,}
287 ⁶⁰, and with RLLs being progressive up to the 2 year follow-up in one of these studies ³⁷.

288

289 Radiolucencies in TKA may be a surrogate marker of aseptic loosening. Loosening is likely to
290 be a progressive process and early RLLs may be a herald of failure at a later stage. Aseptic
291 loosening is the principal cause for early and late revisions, so understanding the rates of RLLs
292 in the ATTUNE TKA and their clinical significance may help guide surgical practice.

293

294 Our results show that despite the high rate of RLLs observed with the original ATTUNE
295 system, the reported rates of loosening within published studies are low. Although, no registry
296 data are available that report specifically on revision due to loosening, in most registries overall
297 revision rates are also low. Overall revision rates of the ATTUNE knee as reported by registries
298 may reasonably be used as an indicator of revision rates for aseptic loosening, unless there
299 were other causes of revision which have lower rates with the ATTUNE. Thus, the clinical
300 significance of high rates of postoperative RLLs in the ATTUNE remains unclear. The
301 observed discrepancy with high rates of RLLs but low reported rates of component loosening
302 or revision may signify that RLLs are not clinically important in the ATTUNE® system.
303 Alternatively, it is possible that RLLs are clinically important but for other reasons their rate
304 of occurrence is not mirrored by loosening and revision rates.

305

306 It is reasonable to expect that rates of RLLs are higher than those of aseptic component
307 loosening which in turn are expected to be higher than revision rates. RLLs do not necessarily
308 equate to loosening and component loosening may not lead to revision surgery. Furthermore,
309 diagnosis of early component loosening in the absence of overt clinical features or significant
310 radiological features such as implant migration or substantial bone loss can be difficult. This
311 diagnosis may be made intra-operatively at the time of revision, but may also be relevant to the
312 substantial proportion of patients who continue with unexplained pain following TKA ¹⁰. In
313 line with such diagnostic challenges, Bonutti et al. reported that 15 patients revised for
314 ATTUNE tibial loosening had developed increasing pain with initiation of weight bearing and
315 loss of active ROM following an initial symptom-free period ¹³. They also reported that all
316 these patients had tenderness on palpation of the medial and lateral part of the tibial plateau
317 and their plain radiographs showed radiolucencies, but they didn't report the presence of overt
318 radiographic evidence of loosening or bone loss. Similar clinical findings of pain and localised
319 tenderness at or just below the joint line were also reported more recently by Murphy et al ⁴⁷
320 in 3 cases of early aseptic failure of the tibial component-cement interface in the ATTUNE
321 prosthesis.

322

323 Even if component aseptic loosening is clear, it is likely that some if not most revisions for this
324 are only carried out when the patient becomes significantly symptomatic. Patients with minor
325 symptoms and no significant bone loss may be monitored rather than proceeding with revision.
326 Assuming this is correct, there will always be a lag between the early stages of a loose
327 component and the reported rates of revision surgery. Moreover, in many healthcare settings
328 such as the UK's National Health System (NHS), there is a further lag between making a
329 decision to carry out revision surgery and actually performing the procedure, with evidence
330 this effect is exacerbated by the backlog due to the COVID-19 pandemic ^{15,28}.

331

332 Although the overall reported loosening and revision rates for the original ATTUNE knee are
333 low, it is notable that there is substantial variation in reported loosening rates between research
334 studies (0 to 16.3%), as well as in overall revision rates reported by registries (2.6% at 5 years
335 in the Australian registry to 5.9% at 5 years in the German registry) ^{48,53}. This variation allied
336 to high rates of RLLs warrants further investigation to fully determine if there is more concern
337 with specific component/design, surgical or cementation technique or patient characteristics.
338 This is also important as registries do not allow clarification of the multiple versions or

339 combinations of an implant and the revision rates for such versions or combinations cannot be
340 easily reviewed ⁴⁹.

341

342 Our study has several limitations. Firstly, the quality of evidence was limited with only one
343 RCT and two prospective cohort studies available ^{37, 51, 57}, the rest being retrospective, and
344 some with no control group. Another limitation was the heterogeneity in the specifics of the
345 ATTUNE® TKA implant with differences in the type of components or cement used. In 4
346 studies that had a control group, the TKA system used as control varied between studies, but,
347 despite this, there was a relative consistency in the findings. We feel this is a valid comparison
348 as it helps demonstrate how the ATTUNE TKA system is performing against a general
349 population of other TKAs performed by the same surgeons, using similar techniques, in similar
350 patient populations. Radiographs can assess RLLs but the technique must follow standard
351 guidelines and fluoroscopic positioning with the beam parallel to the tibia and the components
352 ¹⁸. However, this is operator dependent, and it is difficult to ensure a reproducible technique
353 was used in the analysed studies. Follow-up in most studies was at least 2 years but there was
354 variation in this range and insufficient data to stratify risk of RLLs according to length of
355 follow-up. Examination of earlier years of registry reports before the introduction of the
356 modified tibial tray might have shed some light specifically into the revision rates of the
357 original version of the ATTUNE, but this might be complicated by lower numbers of knees at
358 risk of revision in earlier years.

359

360 The authors believe that despite our study limitations, the original design of the cemented
361 ATTUNE® TKA system is associated with a high rate of RLLs both on the tibia and femur,
362 but it remains unclear specifically which components or bearings are most at risk of this. Whilst
363 we draw attention to this finding we are also unclear of its clinical significance. Longer follow-
364 up studies and data are needed to determine the clinical relevance of the increased rate of RLLs
365 with the original ATTUNE® implant and until such evidence is available, we recommend close
366 surveillance for all patients with this implant.

367

368

369

370 **REFERENCES:**

- 371 1. Australian Orthopaedic Association National Joint Replacement Registry
372 (AOANJRR). Hip, Knee & Shoulder Arthroplasty Annual Report 2022 [Available from:
373 <https://aoanjrr.sahmri.com/annual-reports-2022>.
- 374 2. German Arthroplasty Registry (EPRD). Annual report 2021 [Available from:
375 <https://www.eprd.de/en/downloads/reports>.
- 376 3. Dutch Arthroplasty Register (LROI). Annual report 2022 [Available from:
377 <https://www.lroi-report.nl/>.
- 378 4. Network of Orthopaedic Registries of Europe (NORE). Arthroplasty Registries 2022
379 [Available from: <https://nore.efort.org/arthroplasty-registries>.
- 380 5. Swiss National Joint Registry (SIRIS). SIRIS Annual report 2022 [Available from:
381 <https://www.siris-implant.ch/en/>.
- 382 6. Swiss National Joint Registry (SIRIS). SIRIS Annual report 2021 [Available from:
383 <https://www.siris-implant.ch/en/>.
- 384 7. Arsoy D, Pagnano MW, Lewallen DG, Hanssen AD, Sierra RJ. Aseptic tibial
385 debonding as a cause of early failure in a modern total knee arthroplasty design. *Clin Orthop*
386 *Relat Res.* 2013;471(1):94-101.
- 387 8. Behrend H, Hochreiter B, Potocnik P, El Baz Y, Zdravkovic V, Tomazi T. No
388 difference in radiolucent lines after TKA: a matched-pair analysis of the classic implant and
389 its evolutionary design. *Knee Surg Sports Traumatol Arthrosc.* 2020;28(12):3962-8.
- 390 9. Berend ME, Ritter MA, Hyldahl HC, Meding JB, Redelman R. Implant migration and
391 failure in total knee arthroplasty is related to body mass index and tibial component size. *J*
392 *Arthroplasty.* 2008;23(6 Suppl 1):104-9.
- 393 10. Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of
394 patients report long-term pain after total hip or knee replacement for osteoarthritis? A
395 systematic review of prospective studies in unselected patients. *BMJ Open.*
396 2012;2(1):e000435.
- 397 11. Bhalekar RM, Nargol ME, Shyam N, Nargol AVF, Wells SR, Collier R, et al. Tibial
398 tray debonding from the cement mantle is associated with deformation of the backside of
399 polyethylene tibial inserts. *Bone Joint J.* 2021;103-b(12):1791-801.
- 400 12. Bonutti PM, Khlopas A, Chughtai M, Cole C, Gwam CU, Harwin SF, et al. Unusually
401 High Rate of Early Failure of Tibial Component in ATTUNE Total Knee Arthroplasty
402 System at Implant-Cement Interface. *The journal of knee surgery.* 2017;30(5):435-9.

- 403 13. Bonutti PM, Khlopas A, Chughtai M, Cole C, Gwam CU, Harwin SF, et al. Unusually
404 High Rate of Early Failure of Tibial Component in ATTUNE Total Knee Arthroplasty
405 System at Implant-Cement Interface. *J Knee Surg.* 2017;30(5):435-9.
- 406 14. Buller LT, Rao V, Chiu YF, Nam D, McLawhorn AS. Primary Total Knee
407 Arthroplasty Performed Using High-Viscosity Cement is Associated With Higher Odds of
408 Revision for Aseptic Loosening. *J Arthroplasty.* 2020;35(6s):S182-s9.
- 409 15. Carr A, Smith JA, Camaradou J, Prieto-Alhambra D. Growing backlog of planned
410 surgery due to covid-19. *Bmj.* 2021;372:n339.
- 411 16. Cerquiglini A, Henckel J, Hothi H, Allen P, Lewis J, Eskelinen A, et al. Analysis of
412 the Attune tibial tray backside: A comparative retrieval study. *Bone Joint Res.* 2019;8(3):136-
413 45.
- 414 17. Cerquiglini A, Henckel J, Hothi H, Moser LB, Eskelinen A, Hirschmann MT, et al.
415 Retrieval analysis of contemporary antioxidant polyethylene: multiple material and design
416 changes may decrease implant performance. *Knee surgery, sports traumatology, arthroscopy :*
417 *official journal of the ESSKA.* 2019;27(7):2111-9.
- 418 18. Chalmers BP, Sculco PK, Fehring KA, Taunton MJ, Trousdale RT. Fluoroscopically
419 Assisted Radiographs Improve Sensitivity of Detecting Loose Tibial Implants in Revision
420 Total Knee Arthroplasty. *J Arthroplasty.* 2017;32(2):570-4.
- 421 19. Cheng K, Pruitt L, Zaloudek C, Ries MD. Osteolysis caused by tibial component
422 debonding in total knee arthroplasty. *Clin Orthop Relat Res.* 2006;443:333-6.
- 423 20. Clary CW, Fitzpatrick CK, Maletsky LP, Rullkoetter PJ. The influence of total knee
424 arthroplasty geometry on mid-flexion stability: an experimental and finite element study. *J*
425 *Biomech.* 2013;46(7):1351-7.
- 426 21. Fisher DA, Parkin D. Advancing Patient Outcomes and Economic Value in Total
427 Knee Arthroplasty: The Evidence of the ATTUNE® Knee System 2020 [Available from:
428 [http://synthes.vo.llnwd.net/o16/LLNWMB8/INT%20Mobile/Synthes%20International/Produ](http://synthes.vo.llnwd.net/o16/LLNWMB8/INT%20Mobile/Synthes%20International/Product%20Support%20Material/legacy_Synthes_PDF/125873.pdf)
429 [ct%20Support%20Material/legacy_Synthes_PDF/125873.pdf](http://synthes.vo.llnwd.net/o16/LLNWMB8/INT%20Mobile/Synthes%20International/Product%20Support%20Material/legacy_Synthes_PDF/125873.pdf).
- 430 22. DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemp Clin*
431 *Trials.* 2015;45(Pt A):139-45.
- 432 23. Ewald FC. The Knee Society total knee arthroplasty roentgenographic evaluation and
433 scoring system. *Clin Orthop Relat Res.* 1989(248):9-12.
- 434 24. Foran JR, Whited BW, Sporer SM. Early aseptic loosening with a precoated low-
435 profile tibial component: a case series. *J Arthroplasty.* 2011;26(8):1445-50.

- 436 25. Gallo J, Goodman SB, Konttinen YT, Wimmer MA, Holinka M. Osteolysis around
437 total knee arthroplasty: a review of pathogenetic mechanisms. *Acta Biomater.*
438 2013;9(9):8046-58.
- 439 26. Giaretta S, Berti M, Micheloni GM, Ceccato A, Marangoni F, Momoli A. Early
440 experience with the ATTUNE Total Knee Replacement System. *Acta Biomed.* 2019;90(12-
441 s):98-103.
- 442 27. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al.
443 GRADE: an emerging consensus on rating quality of evidence and strength of
444 recommendations. *Bmj.* 2008;336(7650):924-6.
- 445 28. Haddad FS. Time to call out camouflage. *Bone Joint J.* 2021;103-b(10):1553-4.
- 446 29. Hazelwood KJ, O'Rourke M, Stamos VP, McMillan RD, Beigler D, Robb WJ, 3rd.
447 Case series report: Early cement-implant interface fixation failure in total knee replacement.
448 *Knee.* 2015;22(5):424-8.
- 449 30. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The
450 Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *Bmj.*
451 2011;343:d5928.
- 452 31. Higgins JPT TJ, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors).
453 *Cochrane Handbook for Systematic Reviews of Interventions* version 6.3 (updated February
454 2022): Cochrane; 2022.
- 455 32. Hoskins W, Gorup P, Claireaux H, Stokes C, Bingham R. High incidence of
456 radiolucent lines at the implant-cement interface of a new total knee replacement. *ANZ J*
457 *Surg.* 2020;90(7-8):1299-302.
- 458 33. Indelli PF, Marcucci M, Pipino G, Charlton S, Carulli C, Innocenti M. The effects of
459 femoral component design on the patello-femoral joint in a PS total knee arthroplasty. *Arch*
460 *Orthop Trauma Surg.* 2014;134(1):59-64.
- 461 34. Jaeger S, Eissler M, Schwarze M, Schonhoff M, Kretzer JP, Bitsch RG. Does tibial
462 design modification improve implant stability for total knee arthroplasty? An experimental
463 cadaver study. *Bone Joint Res.* 2022;11(4):229-38.
- 464 35. Jaeger S, Eissler M, Schwarze M, Schonhoff M, Kretzer JP, Bitsch RG. Early tibial
465 loosening of the cemented ATTUNE knee arthroplasty - Just a question of design? *Knee.*
466 2021;30:170-5.
- 467 36. Jin QH, Lee WG, Song EK, Kim WJ, Jin C, Seon JK. No difference in the
468 anteroposterior stability between the GRADIUS and multi-radius designs in total knee
469 arthroplasty. *Knee.* 2020;27(4):1197-204.

- 470 37. Kaptein BL, den Hollander P, Thomassen B, Fiocco M, Nelissen R. A randomized
471 controlled trial comparing tibial migration of the ATTUNE cemented cruciate-retaining knee
472 prosthesis with the PFC-sigma design. *Bone Joint J.* 2020;102-b(9):1158-66.
- 473 38. Kelly BC, Owen JR, Shah SC, Johnson AJ, Golladay GJ, Kates SL. A Biomechanical
474 Comparison of the Effect of Baseplate Design and Bone Marrow Fat Infiltration on Tibial
475 Baseplate Pullout Strength. *J Arthroplasty.* 2021;36(1):356-61.
- 476 39. Kopinski JE, Aggarwal A, Nunley RM, Barrack RL, Nam D. Failure at the Tibial
477 Cement-Implant Interface With the Use of High-Viscosity Cement in Total Knee
478 Arthroplasty. *J Arthroplasty.* 2016;31(11):2579-82.
- 479 40. Lachiewicz PF, Steele JR, Wellman SS. Unexpected high rate of revision of a modern
480 cemented fixed bearing modular posterior-stabilized knee arthroplasty. *Bone Joint J.*
481 2021;103-b(6 Supple A):137-44.
- 482 41. Martin JR, Watts CD, Levy DL, Miner TM, Springer BD, Kim RH. Tibial Tray
483 Thickness Significantly Increases Medial Tibial Bone Resorption in Cobalt-Chromium Total
484 Knee Arthroplasty Implants. *J Arthroplasty.* 2017;32(1):79-82.
- 485 42. Mathes T, Pieper D. Clarifying the distinction between case series and cohort studies
486 in systematic reviews of comparative studies: potential impact on body of evidence and
487 workload. *BMC Med Res Methodol.* 2017;17(1):107.
- 488 43. Meftah M, Ranawat AS, Ranawat CS. Ten-year follow-up of a rotating-platform,
489 posterior-stabilized total knee arthroplasty. *J Bone Joint Surg Am.* 2012;94(5):426-32.
- 490 44. Meneghini RM, Mont MA, Backstein DB, Bourne RB, Dennis DA, Scuderi GR.
491 Development of a Modern Knee Society Radiographic Evaluation System and Methodology
492 for Total Knee Arthroplasty. *J Arthroplasty.* 2015;30(12):2311-4.
- 493 45. Mikulak SA, Mahoney OM, dela Rosa MA, Schmalzried TP. Loosening and
494 osteolysis with the press-fit condylar posterior-cruciate-substituting total knee replacement. *J*
495 *Bone Joint Surg Am.* 2001;83(3):398-403.
- 496 46. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic
497 reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6(7):e1000097.
- 498 47. Murphy JD, Braunlich PR, Judson Iv WR, Harker JN, Baumann PA. Early Aseptic
499 Failure of the Tibial Component-Cement Interface in ATTUNE® Total Knee Arthroplasty: A
500 Report of Three Cases. *Cureus.* 2021;13(12):e20582.
- 501 48. National Joint Registry for England, Wales, Northern Island and the Isle of Man (NJR).
502 19th Annual Report 2022 [Available from: [https://www.njrcentre.org.uk/njr-annual-report-](https://www.njrcentre.org.uk/njr-annual-report-2022/)
503 20222/

- 504 49. Phillips JRA, Tucker K. Implant brand portfolios, the potential for camouflage of
505 data, and the role of the Orthopaedic Data Evaluation Panel in total knee arthroplasty. *Bone*
506 *Joint J.* 2021;103-b(10):1555-60.
- 507 50. Ranawat AS, Ranawat CS, Slamin JE, Dennis DA. Patellar crepitation in the P.F.C.
508 sigma total knee system. *Orthopedics.* 2006;29(9 Suppl):S68-70.
- 509 51. Ranawat CS, White PB, West S, Ranawat AS. Clinical and Radiographic Results of
510 Attune and PFC Sigma Knee Designs at 2-Year Follow-Up: A Prospective Matched-Pair
511 Analysis. *J Arthroplasty.* 2017;32(2):431-6.
- 512 52. DePuy Synthes Joint Reconstruction. Depuy Synthes Joint Reconstruction Introduces
513 Two New Knee Technologies For The ATTUNE® Knee System 2014 [Available from:
514 [https://www.jnj.com/media-center/press-releases/depuy-synthes-joint-reconstruction-](https://www.jnj.com/media-center/press-releases/depuy-synthes-joint-reconstruction-introduces-two-new-knee-technologies-for-the-attune-knee-system)
515 [introduces-two-new-knee-technologies-for-the-attune-knee-system.](https://www.jnj.com/media-center/press-releases/depuy-synthes-joint-reconstruction-introduces-two-new-knee-technologies-for-the-attune-knee-system)
- 516 53. Swedish Knee Arthroplasty Register. Annual report 2020 [Available from:
517 [https://www.myknee.se/en/publications/annual-reports.](https://www.myknee.se/en/publications/annual-reports)
- 518 54. New Zealand Orthopaedic Association Joint Registry. Annual report 2022 [Available
519 from: [https://www.nzoa.org.nz/annual-reports.](https://www.nzoa.org.nz/annual-reports)
- 520 55. Ries C, Heinichen M, Dietrich F, Jakubowitz E, Sobau C, Heisel C. Short-keeled
521 cemented tibial components show an increased risk for aseptic loosening. *Clin Orthop Relat*
522 *Res.* 2013;471(3):1008-13.
- 523 56. Ritter MA, Davis KE, Meding JB, Pierson JL, Berend ME, Malinzak RA. The effect
524 of alignment and BMI on failure of total knee replacement. *J Bone Joint Surg Am.*
525 2011;93(17):1588-96.
- 526 57. Robinson T, King SW, Pilling RW, Aderinto J, Veysi V, Wall O, et al. Attune total
527 knee arthroplasty: is there evidence of early tibial component de-bonding? A prospective
528 cohort study with a minimum two year follow-up. *Journal of Arthroscopy and Joint Surgery.*
529 2021;8(2):139-47.
- 530 58. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological
531 index for non-randomized studies (minors): development and validation of a new instrument.
532 *ANZ J Surg.* 2003;73(9):712-6.
- 533 59. Song SJ, Lee HW, Kang SG, Bae DK, Park CH. Various Types of Medial Tibial Bone
534 Resorption after Total Knee Arthroplasty Using a Thick Cobalt Chromium Tibial Baseplate. *J*
535 *Knee Surg.* 2020.

- 536 60. Staats K, Wannmacher T, Weihs V, Koller U, Kubista B, Windhager R. Modern
537 cemented total knee arthroplasty design shows a higher incidence of radiolucent lines
538 compared to its predecessor. *Knee Surg Sports Traumatol Arthrosc.* 2019;27(4):1148-55.
- 539 61. Torino D, Damsgaard C, Kolessar DJ, Hayes DS, Foster B, Constantino J, et al. Tibial
540 Baseplate-Cement Interface Debonding in the ATTUNE Total Knee Arthroplasty System.
541 *Arthroplast Today.* 2022;17:165-71.
- 542 62. van Loon C, Baas N, Huey V, Lesko J, Meermans G, Vergroesen D. Early outcomes
543 and predictors of patient satisfaction after TKA: a prospective study of 200 cases with a
544 contemporary cemented rotating platform implant design. *J Exp Orthop.* 2021;8(1):30.
- 545 63. Wautier D, Ftaita S, Thienpont E. Radiolucent lines around knee arthroplasty
546 components : a narrative review. *Acta Orthop Belg.* 2020;86(1):82-94.
- 547 64. Wells GA SB, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The
548 Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-
549 analyses 2008 [Available from:
550 http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

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Table 1. Characteristics of all included studies in the systematic review.

Lead author (Year of publication)	Study design (Level of Evidence, Country)	No. of patients (TKAs)	Patient groups (TKA designs, cement used) Group 1: ATTUNE Group 2: Control	Gender (M:F)	Age (years) Mean (range)	Follow-up (months)
Kaptein (2020) ³⁷	RCT (I, Netherlands)	74 (74)	Group 1 (n=38) ATTUNE® CR Fixed Palacos R+G Group 2 (n=36) PFC Sigma® CR Fixed Palacos R+G	Group 1: 18M:20F Group 2: 11M:25F	Group 1: 69±9.5 Group 2: 68±8.2	ATTUNE 24 Control 24
Robinson (2021) ⁵⁷	Prospective cohort (II, UK)	192 (192)	Group 1 (n=96) ATTUNE® CR Fixed Group 2 (n=96) PFC Sigma® CR (n=41) Vanguard® CR (n=55) Fixed Palacos R+G	Group 1: 51M:45F Group 2: 34M:62F NSD	Group 1: 70.6 Group 2: 68.1 P=0.88	ATTUNE 24 Control 24
Ranawat (2017) ⁵¹	Prospective cohort (II, USA)	200 (200)	Group 1 (n=100) ATTUNE® PS 61 fixed / 39 RP Group 2 (n=100) PFC Sigma PS 83 fixed / 17 RP Cement type not specified	Group 1: 33M:67F Group 2: 29M:71F P=0.54	Group 1: 71±7.3 Group 2: 70.1±7.4 P=0.4	ATTUNE Mean: 22.8 (95%CI: 21.6-22.8) Control Mean: 24 (95%CI: 21.6-22.8)
Lachiewicz (2021) ⁴⁰	Retrospective cohort (III, USA)	624 (677)	Group 1 (n=154, 166 TKAs) ATTUNE® PS Fixed, cement: DePuy SmartSet HV: 71 (43%) DePuy SmartSet MV: 77 (46%) Simplex P MV: 18 (11%) Group 2 (n=470, 511 TKAs) Various manufacturers DePuy SmartSet HV: 20 (4%) Simplex-P MV: 492 (96%)	Group 1: 135M:19F Group 2: 419M:51F P=0.784	Group 1: 63.8±8.2 (44-85) Group 2: 64.6±7.7 (43-88) P=0.271	ATTUNE Mean: 23.7±12.4 Range: 6-67 Control Mean: 25±16.8 Range: 10-75

Behrend (2020) ⁸	Retrospective cohort (III, Switzerland)	291 (291)	Group 1 (n=100) ATTUNE® CR Group 2 (n=191) LCS® CR Mobile Palacos R+G	Group 1: 52M:48F Group 2: 85M:106F P=0.22	Group 1: 71±10 (45-89) Group 2: 70±10 (44-91) P=0.68	Both groups Mean: 13.5 Range: 10-21
Jin (2020) ³⁶	Retrospective cohort (III, Korea)	142 (142)	Group 1 (n=68) ATTUNE® PS Group 2 (n=74) PERSONA® PS Fixed Simplex P	Group 1: 9M:59F Group 2: 14M:60F P=0.36	Group 1: 69.7±5.9 Group 2: 67.9±7.3 P=0.44	ATTUNE Mean: 28.4±12.6 Control Mean: 29.1±13.2
Staats (2019) ⁶⁰	Retrospective cohort (III, Austria)	529 (529)	Group 1 (n=276) ATTUNE® 22PS/254CR, 255 fixed / 21 mobile Group 2 (n=253) PFC Sigma® 38PS/215CR Mobile Palacos R+G	Group 1: 103M:173F Group 2: 105M:148F p>0.05	Group 1: 69±9 Group 2: 68±10 p>0.05	ATTUNE Mean: 19±7 Control group Mean: 25±11
Torino (2022) ⁶¹	Case-series (IV, USA)	668 (742)	ATTUNE® CR/PS Fixed or mobile Cement: various types	260M:408F	70.3±9.8	ATTUNE Mean: 42±16.8
van Loon (2021) ⁶²	Case-series (IV, USA)	200 (200)	ATTUNE® RP 115CR/85PS Cement type not specified	74M:126F	65.4±7.8 (41-78)	ATTUNE 24 months
Hoskins (2020) ³²	Case-series (IV, Australia)	112 (122)	ATTUNE® 121 fixed: 9PS/112CR, 1 RP	38M:74F	71.2 (44-89)	ATTUNE Mean: 21 Range: 3-51
Song (2020) ⁵⁹	Case-series (IV, Italy)	500 (500)	ATTUNE® PS Cement type not specified	32M:468F	71.3±7.3	ATTUNE Mean: 40.8±19.2
Giaetta (2019) ²⁶	Case-series (IV, Italy)	185 (192)	ATTUNE® PS Fixed Palacos R+G	89M:129F	70.3±6.52 (43-85)	ATTUNE Mean: 37.9±13.9 Range: 12-64.8

n: number of patients, **TKA:** total knee arthroplasty, **PS:** posterior-stabilised, **CR:** cruciate-retaining, **RP:** rotating-platform, **PFC:** Press-Fit Condylar, **NR:** not reported, **NA:** not applicable, **UK:** United Kingdom **ATTUNE®**, **PFC Sigma®**, **LCS®:** DePuy Synthes, Warsaw, IN, USA. **Vanguard®**, **PERSONA®:** Zimmer Biomet, Warsaw, IN, USA

Table 2. Definition of radiolucency lines (RLL) and radiographic evaluation system in all included studies.

Lead Author (Year)	Definition of RLL	System used for radiographic evaluation (number of assessors)
Kaptein (2020) ³⁷	RLL (tibia) at the implant-cement interface on AP/Lat long-leg standing radiographs.	MKSRESM (2)
	RLL (tibia) either at implant-cement or cement-bone interface on AP/Lat standing radiographs. Reported on both ≥ 2 mm in depth or progressive pattern (significant) and on < 2 mm in depth (non-significant). RLL at implant-cement interface included in analysis.	KSRESM (2)
Ranawat (2017) ⁵¹	RLL (tibia and femur) at implant-cement interface on weight-bearing AP, Lat and 30° merchant view + AP long-leg standing view.	KSRESM (2)
Lachiewicz (2021) ⁴⁰	RLL (tibia) at implant-cement interface on AP/Lat standing radiographs	MKSRESM (2)
Behrend (2020) ⁸	RLL (tibia and femur) at implant-cement interface on AP/Lat radiographs. Documented if ≥ 2 mm in a progressive pattern	MKSRESM
Jin (2020) ³⁶	RLL (tibia and femur) at implant-cement interface on AP/Lat radiographs. Documented if ≥ 2 mm or progressively enlarging RLL was found in any zone in AP/Lat views	KSRESM (2)
Staats (2019) ⁶⁰	RLL (tibia and femur) either at implant-cement or cement-bone interface on AP/Lat standing radiographs. Documented if detected on two serial radiographs	MKSRESM (2)
	RLL (tibia and femur) ≥ 2 mm in depth on AP/Lat standing radiographs	No system reported
Hoskins (2020) ³²	RLL (tibia and femur) at implant-cement interface (AP/Lat radiographs). Classified as partial or complete.	MKSRESM
Song (2020) ⁵⁹	Medial tibial bone resorption was evaluated. Progression according to change in size of bone resorption area, defined as no progression when change in size was less than 2mm.	Own classification system of bone resorption (2)
Giaretta (2019) ²⁶	RLL (tibia and femur) at implant-cement interface on AP/Lat standing radiographs	MKSRESM

RLL: radiolucency lines, **AP:** anteroposterior view, **Lat:** lateral view, **KSRESM:** Knee Society Radiographic Evaluation System²³,

MKSRESM: Modern Knee Society Radiographic Evaluation System⁴⁴

Table 3. Radiolucency lines reported post-operatively in all studies included in the systematic review.*

Lead author (Year)	Type of prosthesis Radiographic evaluation	Tibial RLL (knees) in ATTUNE®	Tibial RLL (knees) in Control	Femoral RLL in ATTUNE®	Femoral RLL in Control	Knees with RLL overall in ATTUNE	Knees with RLL overall in Control	Statistical analysis (ATTUNE vs Control)
Kaptein (2020) ³⁷	ATTUNE vs PFC CR MKSRESM	16 (16) AP Z1: 14 (42%) Z2: 2 (6%)	4 (3) AP Z1: 3 (8.6%) Z2: 1 (2.8%)	NR	NR	16/33 (48%)	3/35 (8.6%)	Tibial/Overall RLL: P=0.002
Robinson (2021) ⁵⁷	ATTUNE vs PFC or Vanguard CR KSRESM	28 (26) AP Z1: 6 (23%) Z4: 2 (7.7%) Lat view Z1: 2 (7.7%) Z2: 2 (7.7%) Z3: 16 (61.5%)	29 (20) AP Z1: 7 (24%) Z3: 1 (3%) Z4: 3 (10%) Lat Z1: 6 (21%) Z2: 2 (7%) Z3: 9 (31%)	NR	NR	26/96 (27%)	20/96 (21%)	Tibia/Overall RLL: P=0.42
Ranawat (2017) ⁵¹	ATTUNE vs PFC PS KSRESM	0/100	0/100	0/100	0/100	0/100	0/100	No difference
Lachiewicz (2021) ⁴⁰	ATTUNE vs various PS MKSRESM	182 (110) AP Z1: 26 (16%) Z2: 14 (8%) Lat Z1: 1 (1%) Z2: 8 (5%) Z3: 3A: 49 (30%) 3P: 28 (17%) Z5: 26 (16%)	NR	NR	NR	110/166 (66%)	NR	NA
Behrend (2020) ⁸	ATTUNE vs LCS CR MKSRESM	2 (1) AP Z1: 1 (1%) Z2: 1 (1%)	6 (5) AP Z1: 2 (1%) Z2: 4 (2.1%)	15 (14) Lat view: Z1: 1 (1%) Z2: 12 (12%) Z3A: 1 (1%) Z3P: 1 (1%)	22 (18) Lat view: Z1: 6 (3.1%) Z2: 15 (7.9%) Z3A: 0 Z3P: 1 (0.5%)	14/100 (14%)	18/191 (9.4%)	Tibial RLL: P=0.428 Femoral RLL: P=0.236 Overall RLL: NSD
Jin (2020) ³⁶	ATTUNE vs PERSONA PS KSRESM	8 (4) AP Z1: 4 (5.9%) Z2: 4 (5.9%)	8 (4) AP Z1: 4 (5.4%) Z2: 4 (5.4%)	6 (3) Lat view: Z1: 3 (4.4%) Z4: 3 (4.4%)	3 (2) Lat view: Z1: 2 (2.7%) Z4: 1 (1.4%)	5/68 (7%)	4/74 (5%)	Tibial RLL: p=0.98 Femoral RLL: p=0.99 Overall RLL: P=0.98

Staats (2019) ⁶⁰	ATTUNE (22PS/254CR) vs PFC (38PS/215CR) MKSRESM	AP 38 (37) Z1: 26 (9%) Z2: 6 (2%) Lat 68 in 56 knees (20.3%) Z1: 6 (2%) Z2: 3 (1%) Z3: 3A: 44 (16%) 3P: 12 (4%) Z5: 3 (1%)	AP 11 (10) Z1: 8 (3%) Z2: 3 (1%) Lat 6 in 6 knees (2.4%) Z1: 0 Z2: 0 Z3: 3A: 3 (1%) 3P: 0 Z5: 3 (1%)	40 (40) Lat view: Z1: 3 (1%) Z2: 33 (12%) Z3: 1	6 (5) Lat view: Z1: 0 Z2: 6 (2%) Z3: 0	97/276 (35%)	19/253 (7.5%)	Tibial RLL: P<0.001 Femoral RLL: P<0.001 Overall RLL: P<0.001
van Loon (2021) ⁶²	ATTUNE RP 115CR/85PS (no control)	0/191	NA	0/191	NA	0/191	NA	NA
Hoskins (2020) ³²	ATTUNE (9PS/112CR) (no control) MKSRESM	AP Z1: 28 (23%) Z2: 28 (23%) Lat Z1: 16 (13%) Z2: 14 (53.8%) Z3: 3A: 0 3P: 1 (3.4%)	NA	Lat view: Z1: 9 (7%) Z2: 0 Z3: 3A: 2 3P: 2 Z5: 17 (14%)	NA	29/122 (23.8%)	NA	NA
Song (2020) ⁵⁹	ATTUNE PS (no control)	21/500 (4.2%) Under medial tibial baseplate UT1: 31 (19.2%) UT2: 10 (2%)	NA	NA	NA	96/500 (19.2%)	NA	NA
Giaretta (2019) ²⁶	ATTUNE PS (no control) MKSRESM	25/192 (13%) AP Any zone: 25 (13%) Lat Any zone: 17 (8.8%)	NA	23/192 (12%) Lat Any zone: 23 (12%)	NA	43/192 (22.4%)	NS	NA

TKA= total knee arthroplasty, PS: posterior-stabilised, CR: cruciate-retaining, RP: rotating-platform, PFC: Press-Fit Condylar, RLL: radiolucency lines, AP: anteroposterior view, Lat: lateral view, Z: zone, NA: not applicable, NR=not reported, NSD=no significant difference, p<0.05: significant, MKSRESM: Modern Knee Society Radiographic Evaluation System ⁴⁴, KSRESM: Knee Society Radiographic Evaluation System ²³, ATTUNE®, PFC Sigma®, LCS®: DePuy Synthes, Warsaw, IN, USA. PERSONA®: Zimmer Biomet, Warsaw, IN, USA

*The numbers in total in each box refer to the numbers of knees which had at least one RLL.

Table 4. Prevalence (estimated rate) for any radiolucency lines in the ATTUNE® groups reported in medial tibia, tibia, femur and overall

RLL (TKA design)	No. of studies (TKAs)	Estimated rate - OR (95% CI)	Estimated rate - OR (95% CI) (excluding the 3 studies reporting on RLL ≥ 2mm) ^{8, 36, 62}	Heterogeneity			
				τ^2	I ²	Q value	P value
Tibia and/or femur overall (fixed)	6 (682)	29.9% (95%CI: 15.6-49.6%)	36.3% (19.6%-57.2%)	1.020	95.182	103.778	P<0.001
Tibia and/or femur overall (CR)	3 (234)	27.4% (13.4-47.9%)	NA	0.535	86.831	15.187	P=0.001
Tibia and/or femur overall (any)	10 (1,558)	21.4%% (95%CI: 12.7-33.7%)	31% (95%CI: 19.2-46%).	0.818	93.708	143.042	P<0.001
Tibia AP (fixed)	5 (560)	27.4% (95%CI: 10.1-55.8%)	36.1% (95%CI: 13.7%-66.8%)	1.794	96.650	119.392	P<0.001
Tibia AP (CR)	3 (234)	18.5% (5.1-49.2%)	NA	1.338	89.688	19.395	P<0.001
Tibia AP (PS)	4 (526)	11.7% (1.8-48.8%)	NA	3.623	97.593	124.653	P<0.001
Tibia AP (any)	9 (1,236)	11.3% (95%CI: 4.5-25.6%)	22.1% (95%CI: 8.7-45.9%)	1.913	95.913	195.721	P<0.001
Medial tibia AP (fixed)	5 (490)	15.8% (95%CI: 8.4-28%)	19% (95%CI: 10-33.1%)	0.562	85.953	28.476	P<0.001
Medial tibia AP (CR)	3 (234)	8.4% (95%CI: 1.0-45.4%)	NA	3.388	93.149	29.193	P<0.001
Medial tibia AP (PS)	4 (834)	8.4% (95%CI: 4.3-15.5%)	NA	0.313	77.971	13.618	P=0.003
Medial tibia AP* (any)	10 (1,666)	9.1% (5.4-15.1%)	12.8% (95%CI: 7.6-20.7)	0.586	86.737	67.859	P<0.001
Tibia Lat (any)	5 (838)	3.8% (95%CI: 1.1-12.1%)	5.6% (95%CI: 1.7-16.7%)	1.447	88.923	36.110	P<0.001
Femur Lat (any)	6 (936)	8.9% (95%CI: 5.1-15%)	11.5% (95%CI: 6.6-19.5%)	0.295	72.982	18.506	P=0.002

RLL: radiolucency lines, **OR:** odds ratio, **95%CI:** 95% Confidence Interval, **p<0.05:** significant, **NA:** not applicable, **TKAs:** total knee arthroplasties, **AP:** anteroposterior view, **Lat:** lateral view, **PS:** Posterior-stabilised, **CR:** cruciate-retaining,

*Medial tibia (AP): included one study which defined as radiolucency any medial tibial bone resorption, but only radiolucencies reported for zones of medial tibial baseplate included⁵⁹

Table 5. Demographics and outcomes (loosening and revision rates) from studies included in the systematic review.

Lead Author (Year)	TKA design	Follow-up (months) Mean (range)	Number of ATTUNE TKAs	Loosening	Revision overall	Revision due to loosening
Robinson (2021) ⁵⁷	Fixed CR	24	96	0	NR	NR
Lachiewicz (2021) ⁴⁰	Fixed PS	Mean: 23.7±12.4 (6-67)	166	27	31*	27*
Jin (2020) ³⁶	Fixed PS	Mean: 28.4±12.6	142	0	NR	NR
Staats (2019) ⁶⁰	Fixed + mobile CR/PS	Mean: 19±7	276	0	3	0
Van Loon (2021) ⁶²	Mobile-CR/PS	Mean: 24	200	NR	1	0
Song (2020) ⁵⁹	PS	Mean: 40.8 (2-5)	500	NR	2	0
Giaretta (2019) ²⁶	Fixed PS	Mean: 37.9 (12-64.8)	228	2	2	2
Torino (2022) ⁶¹	Fixed + mobile	Mean: 42	742	10	17	10

TKA: total knee arthroplasty, **CR:** cruciate-retaining, **PS:** posterior-stabilised, **NR:** not reported
 All were based on radiological findings, with one based on radiological and clinical characteristics ⁴⁰.
 *Including 12 TKAs awaiting revision.

Table 6. Overall revision rates of the ATTUNE TKA reported in National Joint Registries.

NJR (Year)	ATTUNE TKAs (n)	Revisions (n)	Reported revision	Revision rate 1 year (95% CI)	Revision rate 2 years (95% CI)	Revision rate 3 years (95% CI)	Revision rate 4 years (95% CI)	Revision rate 5 years (95% CI)	Revision rate 6 years (95% CI)
UK (2022) ⁴⁸	FB (all fix): 33,769 MB (all fix): 5770	NR	Cumulative	FB (all fix) 0.39 (0.32-0.46) MB (all fix) 0.26 (0.16-0.45)	NR	NR	NR	FB (all fix) 2.06 (1.88-2.27) MB (all fix) 1.37 (1.03-1.83)	NR
Australia (2022) ¹	Cement CR: 20,427 PS: 10,431	CR: 473 PS: 206	Cumulative	CR cement 0.9 (0.9-1.0) PS cement 0.9 (0.7-1.1)	NR	NR	NR	CR cement 3.1 (2.8-3.4) PS cement 2.6 (2.3-3.0)	NR
New Zealand (2022) ⁵⁴	All fix: 35,148	All fix: 193	Rate/100 component years	0.549 (0.474-0.632)	NR	NR	NR	NR	NR
Sweden (2020) ⁵³	All fix: 115	NR	Overall relative risk	0.88 (0.12-6.27)	NR	NR	NR	NR	NR
Germany (2021) ²	CR FB cement 5,802 CR MB cement 1,417 PS FB cement 1,362 PS MB cement 417	NR	Revision probability	CR FB cement 1.6 (1.3-2.0) CR MB cement 1.4 (0.9-2.2) PS FB cement: 2.5 (1.7-3.6) PS MB cement: 1.0 (0.4-2.8)	NR	CR FB cement 3.1 (2.6-3.7) CR MB cement 2.8 (1.9-3.9) PS FB cement: 4.0 (3.0-5.5) PS MB cement: 1.4 (0.6-3.3)	CR FB cement 3.2 (2.7-3.8) CR MB cement 3.2 (2.2-4.6) PS FB cement: 5.6 (4.1-7.6) PS MB cement: 1.4 (0.6-3.3)	CR FB cement 3.6 (2.9-4.4) CR MB cement 3.6 (2.9-4.4) PS FB cement: 5.9 (4.3-8.1) PS MB cement: NR	CR FB cement 3.6 (2.9-4.4) CR MB cement 3.6 (2.9-4.4) PS FB cement: 3.6 (2.9-4.4) PS MB cement: NR
Netherlands (2022) ³	Cement: 3,261	23	Cumulative	0.5 (0.2-0.8)	NR	2.4 (1.7-3.2)	NR	3.2 (2.2-4.1)	NR
Switzerland (2021) ⁶	All fix: 18,286	NR	Cumulative	1.7 (1.5-1.9)	NR	NR	5.7 (5.3-6.1)	6.3 (5.9-6.8)	6.9 (6.3-7.4)

Switzerland (2022) ⁵	All fix CR FB: 2,677 CR MB: 4,753 PS FB: 2,224 PS MB: 3,246	CR FB: 2,677 CR MB: 4,753 PS FB: 2,224 PS FB: 3,246	Adjusted revision rate	NR	CR FB: 2.8 (2.2-3.5) CR MB: 4.2 (3.7-4.9) PS FB: 2.9 (2.3-3.7) PS MB: 3.7 (3.1-4.4)	NR	NR	NR	NR
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NJR: National Joint Registry, **TKA:** total knee arthroplasty, **n:** number, **UK:** United Kingdom, **CR:** cruciate-retaining, **PS:** posterior-stabilised, **FB:** fixed-bearing, **MB:** mobile-bearing, **fix:** fixation, **NR:** not reported.

***Rate/100 component years:** Equivalent to the yearly revision rate expressed as a percent and is derived by dividing the number of prostheses revised by the observed component years multiplied by 100.

****Adjusted revision rate:** Revision rate adjusted for effects of mortality and emigration.

Table 7. Risk of bias for prospective cohort studies using the Newcastle-Ottawa Scale (NOS) ⁶⁴.

Lead author (Year)	Representativeness of cohort	Selection of non-exposed cohort	Ascertainment of exposure	Demonstration of that outcome was not present at start of study	Comparability of cohorts	Assessment of outcome	Follow up long enough for outcomes to occur	Adequate of follow-up of cohorts	NOS score
Robinson (2021) ⁵⁷	Somewhat representative*	Drawn from same community as the exposed cohort*	Secure record*	Yes*	Study control for post-op radiolucencies* Study controls for gender, age, BMI, side, pre-op deformity*	Independent blind assessment*	Yes*	Subject lost to follow-up unlikely to introduce bias – small number lost*	9
Ranawat (2017) ⁵¹	Somewhat representative*	Drawn from same community as the exposed cohort*	Secure record*	Yes*	Study control for post-op radiolucencies* Study controls for gender, age, BMI, side, clinical outcomes, ROM*	Record linkage*	Yes	Subject lost to follow-up unlikely to introduce bias – small number lost*	9

BMI: body mass index, **ROM:** range of motion

A study can be awarded a maximum of 1 star for each question and a maximum of 2 stars for comparability of cohorts. The more stars a study was awarded, the lower was the risk of bias.

Threshold for “Good quality”: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain.

The asterisks represent stars.

Table 8. Assessment of methodological quality of the non-randomised retrospective studies (MINORS criteria) ⁵⁶.

Criteria	Torino (2022) ⁶¹	van Loon (2021) ⁶²	Behrend (2020) ⁸	Jin (2020) ³⁶	van Loon (2021) ⁶²	Staats (2019) ⁶⁰	Hoskins (2020) ³²	Song (2020) ⁵⁹	Giaretta (2019) ²⁶
A clearly stated aim	2	2	2	1	2	2	2	2	2
Inclusion of consecutive patients	0	0	0	0	0	0	0	2	2
Prospective data collection	0	2	2	0	2	0	2	2	0
Endpoints appropriate to the study aim	2	2	2	2	2	2	1	2	2
Unbiased assessment of the study endpoint	1	1	2	2	1	2	1	2	1
Follow-up period appropriate to the study aim	2	2	2	2	2	2	2	2	2
Loss to follow-up <5%	1	2	2	1	2	2	2	2	1
Prospective calculation of the study size	0	0	2	0	2	2	0	2	0
Adequate control group	0	0	2	2	0	2	0	0	0
Contemporary group	2	2	2	2	2	2	2	2	2
Baseline equivalence of groups	2	0	2	2	0	2	0	0	0
Adequate statistical analysis	2	2	2	2	2	2	1	2	1
TOTAL	14	15	22	16	17	20	13	22	13

MINORS, Methodological Index for Non-randomized Studies ⁵⁶.

The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate).

Maximum possible score being 24 for comparative studies.