Safety of orthopedic implants: implant migration analysis a must

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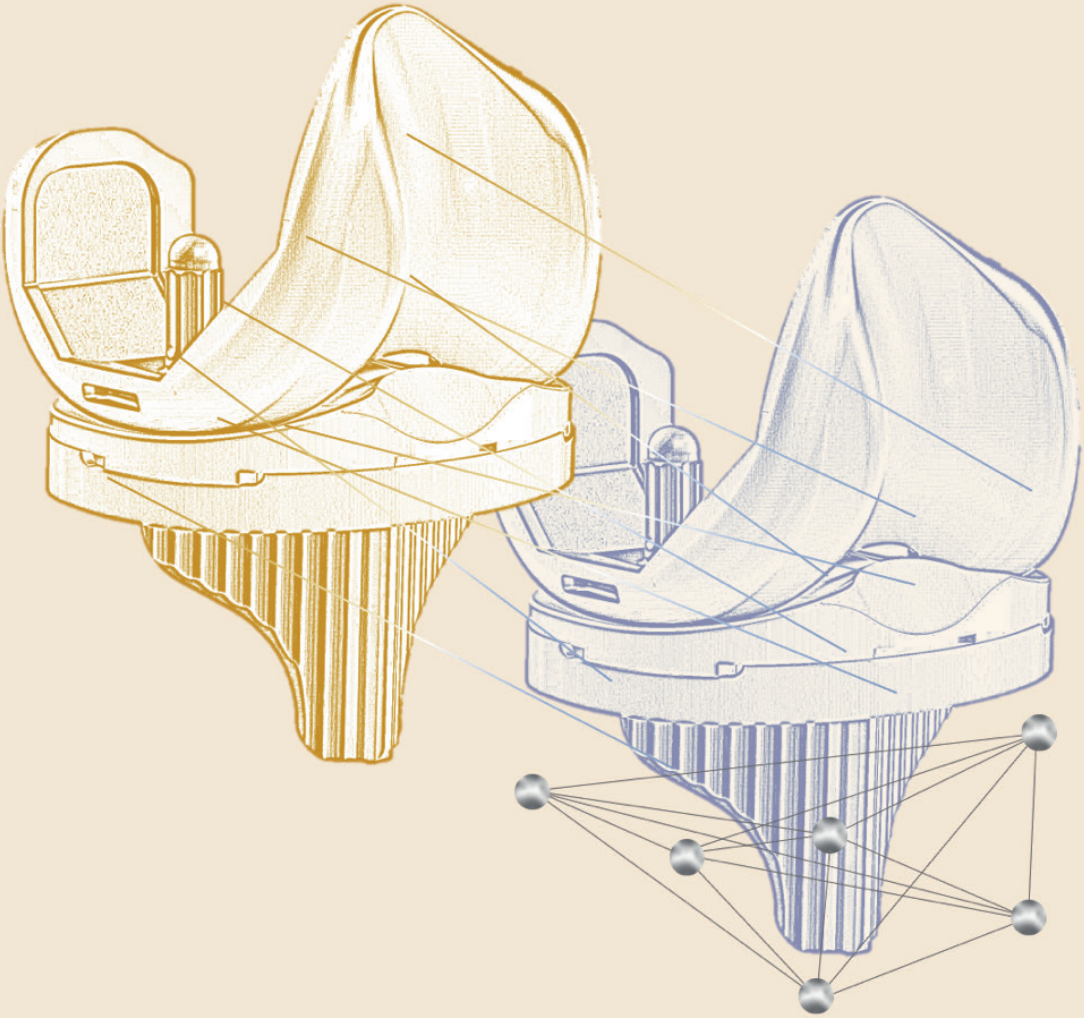

Chapter IX

General Discussion and Future Perspectives

Total knee arthroplasties (TKAs) have excellent short- and long-term results considering its low revision rates which are 4 - 6% at ten years and 8-10% at 20 years, and patient reported outcome measures (PROMs) are good to excellent in the majority of patients.[1-11] Even though TKA designs have achieved these excellent results for the last 3 decades, the results are less favourable in a subgroup of patients. For that matter in patients younger than 60 years the lifetime risk for a revision is 30% and up to 15-20% of these relative young patients are not satisfied with their overall outcome.[5-11] For these reasons, novel TKA designs are introduced on a regular basis. However, clinical evidence supporting superiority of these novel designs is frequently lacking.[12] Concerns on implants being introduced onto the market without sufficient clinical evidence have increased, particularly after some medical devices created disasters to patients, like the metal-on-metal hip prostheses in orthopaedics and the PIP-breast implants and vaginal meshes in other fields.[13-16] The metal-on-metal hip prostheses were introduced with the promise that they would benefit younger and more active patients.[17, 18] Short-term results of these prostheses were promising, but then studies reported pseudo-tumours, an adverse reaction to metal debris, which lead to up to fourfold increased revision rates in young patients as reported by the Australian Registry and NORE (Network of Orthopaedic Registries of Europe). [19-24] These bad outcomes in total hip as well as worse performance for some total knee implants stress again the necessity of a phased introduction of new implants as has been advocated for several decades.[15, 24-27]

To prevent these less favourable outcomes in patients, the EU commission implemented the medical device regulation (MDR) in 2017, which became effective in 2021.[28-30] The main difference between the medical devices directive (MDD) and the MDR included: 1) stricter requirements of clinical evidence for access to the EU market, including post-market surveillance, 2) a comprehensive EU database of high-risk medical devices and its adverse events (EUDAMED), and 3) independent

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expert panels to evaluate new medical devices who need to be consulted on these high-risk medical devices. The "new" requirements of clinical evidence prior to market introduction has been suggested for decades.[27, 31-34] Pre-market studies ideally subject a minimum number of patients to a novel implant while providing objective strong evidence on their performance. In orthopaedics, evaluating clinical results of novel implants can be challenging as the primary outcome often involves all-cause revision, which is relatively rare for orthopaedic hip and knee implants within the first ten years. Due to the low frequency of occurrences, large patient cohorts with extensive follow-up are required to gather sufficient clinical evidence to demonstrate the superiority of a novel implant design. Since loosening of the implant within the supporting bone is the major reason for failure, revision due to loosening is the main endpoint when evaluating orthopaedic implants. Thus, methods providing objective results on implant fixation are most important for evaluating new implants in the pre-market evaluation phase, ideally with an objective and highly accurate technique requiring a minimum of patients to be exposed to the new implant.
Radiostereometric analysis (RSA), which measures implant migration, is such a method as it can identify implants at risk of aseptic loosening as early as one- or two-year follow-up.[35, 36] It does so by measuring implant migration with high accuracy (up to 0.1mm and rotation up to 0.1°).[37] Implants with high initial or continuous migration after one year are known to be prone to failure.[35, 36] Therefore, RSA is an ideal tool to assess novel implants prior to massive market introduction.

This thesis contributes to the existing literature by expanding our understanding of TKAs performance by measuring implant migration using RSA at two-, five- and ten-year follow-up. Furthermore, this thesis conducted a comprehensive pooled analysis to examine the impact of surgical alignment on implant migration. Additionally, the present thesis explored alternative biomarkers of implant migration, which have potential to serve as early indicators for detecting implant loosening. Presented studies in this thesis strengthen the importance of highly accurate measurement tools of implant migration for providing short-term clinical evidence on the

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performance of TKA implants, to ensure the best possible outcomes for patients in the long run.

Migration thresholds

If RSA would be used to evaluate implants prior to market entry, the key question is when is early migration too high, i.e., which migration threshold is clinically relevant for long-term performance. In this thesis, we used the threshold proposed by Ryd et al. (1995) to assess the number of implants at risk for early aseptic loosening, defined as an increase of 0.2 mm MTPM or more between one year and two years of follow-up.[35] This threshold dates from 1995 and was determined by assessing 158 patients who had different TKA implants with either cemented or uncemented designs (N = 120) or even UKAs (N = 38). In this series 15 implants (14 TKAs; 1 UKA) were revised for mechanical loosening of the tibial component within 1 to 11 years after the primary surgery. All the revised implants showed continuous migration over time and had higher migration at one year compared to the control group (i.e., non-revised implants). The authors used the difference in migration between both groups to define thresholds as >0.2 mm MTPM migration between one year and two years. In **Chapter IV**, **Chapter V**, and **Chapter VI**, we used this threshold to identify the number of continuously migrating implants for the different types of design i.e., MBT and APT designs, and for cemented and 3D-printed uncemented designs. We also used this threshold to identify the number of continuously migrating implants for postoperative in-range (femorotibial angle of 0° ±3°) and out-of-range (femorotibial angle of <-3° or +3°) TKAs (**Chapter VIII**). In a post-hoc analysis, the number of continuously migrating implants were similar in these studies for the different implant designs, and for postoperative in-range and out-of-range TKAs. Given that these migration thresholds date from nearly three decades ago in a very heterogenous group of knee implants and considering the substantial improvements in implant design and fixation methods since then, it is important to conduct mid- and long-term RSA studies to assess the external validity of predictions regarding continuously migrating implants made at two years as every implant design is likely to have a distinct migration profile. In **Chapter VI**, we contribute further evidence on this matter by investigating whether continuously migrating implants at two years continued to migrate up to five years postoperatively. We found that one TKA was revised due to continuous migration, four showed late stabilization and four could not been analysed due to missing data at five years. These results suggest that implants can stabilize after an initial period of continuous migration and highlight the importance of five- and 10-year follow-up in RSA studies to assess long-term migration profiles of different TKA designs. This raises the question whether long-term results should be considered in a phased introduction of novel implants. Incorporating long-term results would negate the advantage of RSA studies, which provides early (i.e., at two years) insights into the migration profile of a novel implant, but they may be required for implants with progressive migration at two years.

Furthermore, it should be noted that the a-priori chance of developing aseptic loosening of the tibial component in the study by Ryd et al. (1995) was about 10% at ten years.[35] The chance of all cause revision has since then decreased to approximately 5% at 10 years of which approximately 20% is due to tibial loosening.[1] This small a-priori risk of tibial loosening of TKA implies that large patient cohorts are needed to validate the threshold proposed by Ryd et al.[35] In this context, we increased the sample size by combining data from ten RSA studies comprising 636 TKAs at baseline (**Chapter VIII**). However, when the revision rate is around 1% at 10 years, this would require approximately 1500 TKAs (across RSA studies) to be included to have 15 revisions due to tibial loosening and to compare the migration of these revised TKAs to non-revised TKAs. The latter implies that network analysis across RSA centres and sharing individual patient data is the way forward.[38, 39] Ideally, a global registry of RSA studies should be established, for example by The International Radiostereometry Society.

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Surgical alignment technique influencing migration

Besides using RSA to assess novel implants prior to market introduction, RSA can also be used to evaluate the effect of surgical techniques on implant migration. Traditionally, orthopaedic surgeons aim for neutral coronal alignment (i.e., mechanical alignment hip-knee-ankle angle or femorotibial angle is 0 degrees).[40] While this 'one size fits all' principle has resulted in low revision rates for modern TKAs, the number of patients who are not satisfied after TKA is 15-20%, which is higher compared to total hip arthroplasty.[41] Possible reasons for patients not being satisfied include the management of patient expectations but could also be that the TKA prosthesis is neutrally aligned even in patients who had a preoperative varus or valgus knee alignment. This is a substantial group as the native knee alignment in men and women is varus in 32% and 17%, respectively.[40] Changing the alignment of these patients to neutral, could result in a change in soft tissue balance, which may cause an unnatural feeling of the knee.[40] Other alignment principles have been proposed, like kinematic alignment, which aims to insert the knee implants in a similar fashion as the preoperative alignment.[40] Proponents of this technique state that this alignment technique respects the soft-tissue balance and requires less soft-tissue releases to balance the TKA.[42-44] By respecting the preoperative alignment and the native soft-tissue balance, patients could experience their 'new' knee as more natural which theoretically could increase patient satisfaction. But the reality is more complex than just focussing on individual preoperative alignment as varus positioning of TKA could cause more migration and in turn more loosening in the long term.[45, 46]

In the past years, several variations to kinematic alignment have been introduced such as "kinematic alignment plus" or "mild kinematic alignment".[47, 48] These variants have the same principles as kinematic alignment but differ slightly in terms of the acceptable amount of varus or valgus. Opponents of this technique state that malalignment (i.e., varus or valgus alignment) could result in an unfavourable load transfer through the implant which in turn could increase the risk of loosening and revision.[40, 49-53] Research in this thesis contributes to this debate. We showed that failing to achieve postoperative neutral mechanical alignment did not affect tibial migration up to two years in patients with a preoperative varus or valgus aligned knee (**Chapter VIII**). Therefore, our findings suggest that postoperative varus or valgus aligned TKAs do not have an increased risk of failure due to aseptic loosening in contrast to prior findings of van Hamersveld et al. (2019) who found increased migration of postoperative varus aligned TKAs.[46] Difference between both studies was however that we excluded preoperative neutrally aligned knees and therefore only assessed preoperative varus and valgus aligned knees. For these patients, postoperative neutral, varus or valgus alignment was not related to increased implant migration. Our study suggests that kinematic alignment could thus be a safe treatment option as it does not increase the risk of aseptic loosening but has the advantage that it requires less soft tissue release. Unfortunately, we did not assess functional outcome nor patient reported outcome measures (PROMs) in our study so that we could not test whether kinematic alignment resulted in better patient satisfaction. Another limitation of our study was that the aim of TKA positioning was neutral mechanical alignment and any deviation from neutral postoperative alignment was due to a combination of random variation as well as intra-operative assessment of the soft tissue balance by the orthopedic surgeon, making it difficult to assess a causal relationship in our study.

Other studies report ambiguous results regarding postoperative patient satisfaction and function, with some studies suggesting better clinical outcomes following kinematic alignment and others suggesting no difference between both alignment principles.[48, 54-58] These findings also highlight the complexity of determining the optimal alignment for an individual patient when this is based only on PROMs and functional outcome. For that matter functional outcome and survival of TKAs are influenced by many other factors besides coronal alignment, like preoperative expectations, preoperative functionality and kinematics.[59] So what the optimal

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coronal and sagittal alignment should be for an individual patient in order to have good long-term bone-implant fixation as well as subjective outcomes is determined by a complex of multifactorial variables. Novel techniques aimed at improving the precision of implant positioning, such as robot-assisted surgery, machine learning algorithms or AI, may prove advantageous, but they still need to undergo validation through implant migration analysis studies and other clinical research.[60-64]

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Future perspectives

In recent years, both implant design and measurement techniques of implant performance, like implant migration techniques, have improved considerable and in turn have improved implants and thus patient safety and outcomes. Biomarkers for example could monitor or identify implants at risk for loosening. Furthermore, an improvement in implant migration assessment could be the development of CT-based RSA, which has emerged as a promising technique in implant-bone migration assessment.[65-68] Last, the introduction of 3D-printing technology has enabled the creation of customized and patient-centred implants, but whether this is favourable in the long run for implant fixation, also has to be shown by implant migration studies.[69]

An early warning signal

As mentioned earlier, TKAs have an excellent survival of approximately 94-96% at ten-years.[1, 2] Although the risk of TKA failure is low, it is associated with severe morbidity and frequently results in extensive revision surgery.[70 71] This low revision rate in the overall TKA population, but not in the younger population (e.g., 60 years), makes it difficult to improve outcomes. Where RSA can only be used in specific and a limited number of patients, it is frequently only used in patients included in studies. It also requires additional steps intra-operatively, in contrast with other biological markers that could be assessed relatively easy in large patient cohorts. This thesis contributes further evidence by demonstrating that serum tumour necrosis factor α (TNFα), serum interleukin-1b (IL-1b), serum osteocalcin, and urinary N-terminal telopeptide (NTX) were significantly increased in loosened implants compared with stable implants at time of diagnosis or prior to revision surgery (**Chapter III**). These findings suggest that these biomarkers may have the potential to act as early indicators for loosened implants, as well as for monitoring progression of loosening.[72, 73] Advantages of such biomarkers are: first, sampling from patients with implant-related complaints, thus differentiating between

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implant-bone interface problems (e.g. loosening), soft-tissue problems, infection or other factors. Also, longitudinal studies could establish biomarker values that predict loosening. If the association between specific biomarker levels and implant loosening is further confirmed, these biomarkers could be used to monitor treatment modalities aimed at preventing or delaying implant loosening, like gene-directed therapy to fixate loosened implants or the use of bisphonates.[74-77]

To conclude

No innovation without evaluation is a common saying. In the case of new implant designs, evaluation should include clinical studies prior to market introduction among which implant migration studies (e.g., RSA studies). The latter safeguards good implants and thereby, enabling good to excellent patient outcomes.

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References

1. LROI, Dutch Artrhoplasty Register. Online LROI annual report 2022. Available from: https://www.lroi-report.nl. Accessed on 21-08-2023.
2. NJR NJR. 17th Annual Report 2020. Available from: https://reports.njrcentre.org.uk/Portals/0/PDFdownloads/NJR%2017th%20Annual%20Report%202020.pdf. Accessed on 08-02-2021.
3. Liddle AD, Pandit H, Judge A, Murray DW. Patient-reported outcomes after total and unicompartmental knee arthroplasty: a study of 14,076 matched patients from the National Joint Registry for England and Wales. Bone Joint J. 2015 97-b(6):793-801 DOI: 10.1302/0301-620x.97b6.35155.
4. Australian Orthopaedic Association National Joint Replacement Registry. Annual Report 2020 Hip, Knee & Shoulder Arthroplasty. Available from: https://aoanjrr.sahmri.com/documents/10180/689619/Hip%2C+Knee+%26+Shoulder+Arthroplasty+New/6a07a3b8-8767-06cf-9069-d165dc9baca7. Accessed on April 14, 2021.
5. Nilsdotter AK, Toksvig-Larsen S, Roos EM. Knee arthroplasty: are patients' expectations fulfilled? A prospective study of pain and function in 102 patients with 5-year follow-up. Acta Orthop. 2009 80(1):55-61 DOI: 10.1080/17453670902805007.
6. Leichtenberg CS, Vliet Vlieland TPM, Kroon HM, Dekker J, Marijnissen WJ, Damen PJ, et al. Self-reported knee instability associated with pain, activity limitations, and poorer quality of life before and 1 year after total knee arthroplasty in patients with knee osteoarthritis. J Orthop Res. 2018 36(10):2671-2678 DOI: 10.1002/jor.24023.
7. Tilbury C, Haanstra TM, Leichtenberg CS, Verdegaal SH, Ostelo RW, de Vet HC, et al. Unfulfilled Expectations After Total Hip and Knee Arthroplasty Surgery: There Is a Need for Better Preoperative Patient Information and Education. J Arthroplasty. 2016 31(10):2139-45 DOI: 10.1016/j.arth.2016.02.061.
8. Keurentjes JC, Fiocco M, So-Osman C, Onstenk R, Koopman-Van Gemert AW, Pöll RG, et al. Patients with severe radiographic osteoarthritis have a better prognosis in physical functioning after hip and knee replacement: a cohort-study. PLoS One. 2013 8(4):e59500 DOI: 10.1371/journal.pone.0059500.
9. Barlow T, Clark T, Dunbar M, Metcalfe A, Griffin D. The effect of expectation on satisfaction in total knee replacements: a systematic review. Springerplus. 2016 5:167 DOI: 10.1186/s40064-016-1804-6.
10. Bayliss LE, Culliford D, Monk AP, Glyn-Jones S, Prieto-Alhambra D, Judge A, et al. The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study. Lancet. 2017 389(10077):1424-1430 DOI: 10.1016/s0140-6736(17)30059-4.
11. Bourne RB, Chesworth BM, Davis AM, Mahomed NN, Charron KD. Patient satisfaction after total knee arthroplasty: who is satisfied and who is not? Clin Orthop Relat Res. 2010 468(1):57-63 DOI: 10.1007/s11999-009-1119-9.
12. Nieuwenhuijse MJ, Nelissen RG, Schoones JW, Sedrakyan A. Appraisal of evidence base for introduction of new implants in hip and knee replacement: a systematic review of five widely used device technologies. Bmj. 2014 349:g5133 DOI: 10.1136/bmj.g5133.
13. Sedrakyan A. Metal-on-metal failures--in science, regulation, and policy. Lancet. 2012 379(9822):1174-6 DOI: 10.1016/s0140-6736(12)60372-9.
14. Martindale V, Menache A. The PIP scandal: an analysis of the process of quality control that failed to safeguard women from the health risks. J R Soc Med. 2013 106(5):173-7 DOI: 10.1177/0141076813480994.
15. Keogh B. Poly Implant Prostheses (PIP) Breast Implants: Final Report of the expert group. 2012.
16. O'Neill J. Lessons from the vaginal mesh scandal: enhancing the patient-centric approach to informed consent for medical device implantation. Int J Technol Assess Health Care. 2021 37(1):e53 DOI: 10.1017/s0266462321000258.
17. Cuckler JM. The rationale for metal-on-metal total hip arthroplasty. Clin Orthop

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Relat Res. 2005 441:132-6 DOI: 10.1097/01.blo.0000193809.85587.f8.
18. Fisher J, Jin Z, Tipper J, Stone M, Ingham E. Tribology of alternative bearings. Clin Orthop Relat Res. 2006 453:25-34 DOI: 10.1097/01.blo.0000238871.07604.49.
19. Pandit H, Glyn-Jones S, McLardy-Smith P, Gundle R, Whitwell D, Gibbons CL, et al. Pseudotumours associated with metal-on-metal hip resurfacings. J Bone Joint Surg Br. 2008 90(7):847-51 DOI: 10.1302/0301-620x.90b7.20213.
20. Wynn-Jones H, Macnair R, Wimhurst J, Chirodian N, Derbyshire B, Toms A, et al. Silent soft tissue pathology is common with a modern metal-on-metal hip arthroplasty. Acta Orthop. 2011 82(3):301-7 DOI: 10.3109/17453674.2011.579518.
21. Langton DJ, Sidaginamale RP, Joyce TJ, Natu S, Blain P, Jefferson RD, et al. The clinical implications of elevated blood metal ion concentrations in asymptomatic patients with MoM hip resurfacings: a cohort study. BMJ Open. 2013 3(3) DOI: 10.1136/bmjopen-2012-001541.
22. Drummond J, Tran P, Fary C. Metal-on-Metal Hip Arthroplasty: A Review of Adverse Reactions and Patient Management. J Funct Biomater. 2015 6(3):486-99 DOI: 10.3390/jfb6030486.
23. Pijls BG, Meessen JM, Schoones JW, Fiocco M, van der Heide HJ, Sedrakyan A, et al. Increased Mortality in Metal-on-Metal versus Non-Metal-on-Metal Primary Total Hip Arthroplasty at 10 Years and Longer Follow-Up: A Systematic Review and Meta-Analysis. PLoS One. 2016 11(6):e0156051 DOI: 10.1371/journal.pone.0156051.
24. Pijls BG, Meessen J, Tucker K, Stea S, Steenbergen L, Marie Fenstad A, et al. MoM total hip replacements in Europe: a NORE report. EFORT Open Rev. 2019 4(6):423-429 DOI: 10.1302/2058-5241.4.180078.
25. Malchau H. On the importance of stepwise introduction of new hip implant technology: Assessment of total hip replacement using clinical evaluation, radiostereometry, digitized radiography and a national hip registry [Thesis]. Göteborg, Sweden: Göteborg University. 1995.
26. Nelissen RG, Pijls BG, Kärrholm J, Malchau H, Nieuwenhuijse MJ, Valstar ER. RSA and registries: the quest for phased introduction of new implants. J Bone Joint Surg Am. 2011 93 Suppl 3:62-5 DOI: 10.2106/jbjs.K.00907.
27. Huiskes R. Failed innovation in total hip replacement. Diagnosis and proposals for a cure. Acta Orthop Scand. 1993 64(6):699-716 DOI: 10.3109/17453679308994602.
28. European Union. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0745&from=EN. Accessed on 22 December, 2021.
29. Thienpont E, Quaglio G, Karapiperis T, Kjaersgaard-Andersen P. Guest Editorial: New Medical Device Regulation in Europe: A Collaborative Effort of Stakeholders to Improve Patient Safety. Clin Orthop Relat Res. 2020 478(5):928-930 DOI: 10.1097/corr.0000000000001154.
30. Fraser AG, Nelissen R, Kjærsgaard-Andersen P, Szymański P, Melvin T, Piscoi P. Improved clinical investigation and evaluation of high-risk medical devices: the rationale and objectives of CORE-MD (Coordinating Research and Evidence for Medical Devices). EFORT Open Rev. 2021 6(10):839-849 DOI: 10.1302/2058-5241.6.210081.
31. Nelissen RG, Pijls BG, Karrholm J, Malchau H, Nieuwenhuijse MJ, Valstar ER. RSA and registries: the quest for phased introduction of new implants. J Bone Joint Surg Am. 2011 93:62-5 DOI: 10.2106/jbjs.k.00907.
32. Malchau H. Introducing new technology: a stepwise algorithm. Spine (Phila Pa 1976). 2000 25(3):285 DOI: 10.1097/00007632-200002010-00004.
33. Malchau H, Garellick G, Berry D, Harris WH, Robertson O, Karrlholm J, et al. Arthroplasty implant registries over the past five decades: Development, current, and future impact. J Orthop Res. 2018 36(9):2319-2330 DOI: 10.1002/jor.24014.
34. Sedrakyan A, Campbell B, Merino JG, Kuntz R, Hirst A, McCulloch P. IDEAL-D: a rational framework for evaluating and

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regulating the use of medical devices. Bmj. 2016 353:i2372 DOI: 10.1136/bmj.i2372.
35. Ryd L, Albrektsson BE, Carlsson L, Dansgard F, Herberts P, Lindstrand A, et al. Roentgen stereophotogrammetric analysis as a predictor of mechanical loosening of knee prostheses. J Bone Joint Surg Br. 1995 77(3):377-83.
36. Pijls BG, Valstar ER, Nouta KA, Plevier JW, Fiocco M, Middeldorp S, et al. Early migration of tibial components is associated with late revision: a systematic review and meta-analysis of 21,000 knee arthroplasties. Acta Orthop. 2012 83(6):614-24 DOI: 10.3109/17453674.2012.747052.
37. Selvik G. Roentgen stereophotogrammetry. A method for the study of the kinematics of the skeletal system. Acta Orthop Scand Suppl. 1989 232:1-51.
38. Sedrakyan A, Paxton EW, Phillips C, Namba R, Funahashi T, Barber T, et al. The International Consortium of Orthopaedic Registries: overview and summary. J Bone Joint Surg Am. 2011 93 Suppl 3:1-12 DOI: 10.2106/jbjs.K.01125.
39. Sedrakyan A, Paxton EW, Marinac-Dabic D. Stages and tools for multinational collaboration: the perspective from the coordinating center of the International Consortium of Orthopaedic Registries (ICOR). J Bone Joint Surg Am. 2011 93 Suppl 3:76-80 DOI: 10.2106/jbjs.K.01141.
40. Bellemans J, Colyn W, Vandenneucker H, Victor J. The Chitranjan Ranawat award: is neutral mechanical alignment normal for all patients? The concept of constitutional varus. Clin Orthop Relat Res. 2012 470(1):45-53 DOI: 10.1007/s11999-011-1936-5.
41. Matsuda S, Kawahara S, Okazaki K, Tashiro Y, Iwamoto Y. Postoperative alignment and ROM affect patient satisfaction after TKA. Clin Orthop Relat Res. 2013 471(1):127-33 DOI: 10.1007/s11999-012-2533-y.
42. Oussedik S, Abdel MP, Cross MB, Haddad FS. Alignment and fixation in total knee arthroplasty: changing paradigms. Bone Joint J. 2015 97-b(10 Suppl A):16-9 DOI: 10.1302/0301-620x.97b10.36499.
43. Howell SM, Howell SJ, Kuznik KT, Cohen J, Hull ML. Does a kinematically aligned total knee arthroplasty restore function without failure regardless of alignment category? Clin Orthop Relat Res. 2013 471(3):1000-7 DOI: 10.1007/s11999-012-2613-z.
44. MacDessi SJ, Griffiths-Jones W, Chen DB, Griffiths-Jones S, Wood JA, Diwan AD, et al. Restoring the constitutional alignment with a restrictive kinematic protocol improves quantitative soft-tissue balance in total knee arthroplasty: a randomized controlled trial. Bone Joint J. 2020 102-b(1):117-124 DOI: 10.1302/0301-620x.102b1.Bjj-2019-0674.R2.
45. Hasan S, Kaptein BL, Nelissen R, van Hamersveld KT, Toksvig-Larsen S, Marang-van de Mheen PJ. The Influence of Postoperative Coronal Alignment on Tibial Migration After Total Knee Arthroplasty in Preoperative Varus and Valgus Knees: A Secondary Analysis of 10 Randomized Controlled Trials Using Radiostereometric Analysis. J Bone Joint Surg Am. 2021 DOI: 10.2106/jbjs.20.01659.
46. van Hamersveld KT, Marang-van de Mheen PJ, Nelissen R. The Effect of Coronal Alignment on Tibial Component Migration Following Total Knee Arthroplasty: A Cohort Study with Long-Term Radiostereometric Analysis Results. J Bone Joint Surg Am. 2019 101(13):1203-1212 DOI: 10.2106/jbjs.18.00691.
47. Riviere C, Iranpour F, Auvinet E, Howell S, Vendittoli PA, Cobb J, et al. Alignment options for total knee arthroplasty: A systematic review. Orthop Traumatol Surg Res. 2017 103(7):1047-1056 DOI: 10.1016/j.otsr.2017.07.010.
48. Oussedik S, Abdel MP, Victor J, Pagnano MW, Haddad FS. Alignment in total knee arthroplasty. Bone Joint J. 2020 102-b(3):276-279 DOI: 10.1302/0301-620x.102b3.Bjj-2019-1729.
49. Jeffery RS, Morris RW, Denham RA. Coronal alignment after total knee replacement. J Bone Joint Surg Br. 1991 73(5):709-14.
50. Fang DM, Ritter MA, Davis KE. Coronal alignment in total knee arthroplasty: just how important is it? J Arthroplasty. 2009 24(6 Suppl):39-43 DOI: 10.1016/j.arth.2009.04.034.
51. Abdel MP, Oussedik S, Parratte S, Lustig S, Haddad FS. Coronal alignment in total knee replacement: historical review, contemporary analysis, and future direction. Bone Joint J. 2014 96-b(7):857-62 DOI: 10.1302/0301-620x.96b7.33946.

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52. Parratte S, Pagnano MW, Trousdale RT, Berry DJ. Effect of postoperative mechanical axis alignment on the fifteen-year survival of modern, cemented total knee replacements. J Bone Joint Surg Am. 2010 92(12):2143-9 DOI: 10.2106/jbjs.i.01398.
53. Ritter MA, Davis KE, Meding JB, Pierson JL, Berend ME, Malinzak RA. The effect of alignment and BMI on failure of total knee replacement. J Bone Joint Surg Am. 2011 93(17):1588-96 DOI: 10.2106/jbjs.j.00772.
54. Wen L, Wang Z, Ma D, Zhao X. An early clinical comparative study on total knee arthroplasty with kinematic alignment using specific instruments versus mechanical alignment in varus knees. Front Surg. 2022 9:1097302 DOI: 10.3389/fsurg.2022.1097302.
55. Nam D, Nunley RM, Barrack RL. Patient dissatisfaction following total knee replacement: a growing concern? Bone Joint J. 2014 96-b(11 Supple A):96-100 DOI: 10.1302/0301-620x.96b11.34152.
56. Dossett HG, Estrada NA, Swartz GJ, LeFevre GW, Kwasman BG. A randomised controlled trial of kinematically and mechanically aligned total knee replacements: two-year clinical results. Bone Joint J. 2014 96-b(7):907-13 DOI: 10.1302/0301-620x.96b7.32812.
57. Van Essen J, Stevens J, Dowsey MM, Choong PF, Babazadeh S. Kinematic alignment results in clinically similar outcomes to mechanical alignment: Systematic review and meta-analysis. Knee. 2023 40:24-41 DOI: 10.1016/j.knee.2022.11.001.
58. Lung BE, Donnelly MR, McLellan M, Callan K, Amirhekmat A, McMaster WC, et al. Kinematic Alignment May Reduce Opioid Consumption and Length of Stay Compared to Mechanically Aligned Total Knee Arthroplasty. Orthop Surg. 2023 15(2):432-439 DOI: 10.1111/os.13605.
59. van Diemen MPJ, Ziagkos D, Kruizinga MD, Bénard MR, Lambrechtse P, Jansen JAJ, et al. Mitochondrial function, grip strength, and activity are related to recovery of mobility after a total knee arthroplasty. Clin Transl Sci. 2023 16(2):224-235 DOI: 10.1111/cts.13441.
60. Deckey DG, Rosenow CS, Verhey JT, Brinkman JC, Mayfield CK, Clarke HD, et al. Robotic-assisted total knee arthroplasty improves accuracy and precision compared to conventional techniques. Bone Joint J. 2021 103-b(6 Supple A):74-80 DOI: 10.1302/0301-620x.103b6.Bjj-2020-2003.R1.
61. Jones CW, Jerabek SA. Current Role of Computer Navigation in Total Knee Arthroplasty. J Arthroplasty. 2018 33(7):1989-1993 DOI: 10.1016/j.arth.2018.01.027.
62. Song EK, Seon JK, Yim JH, Netravali NA, Bargar WL. Robotic-assisted TKA reduces postoperative alignment outliers and improves gap balance compared to conventional TKA. Clin Orthop Relat Res. 2013 471(1):118-26 DOI: 10.1007/s11999-012-2407-3.
63. Liow MH, Xia Z, Wong MK, Tay KJ, Yeo SJ, Chin PL. Robot-assisted total knee arthroplasty accurately restores the joint line and mechanical axis. A prospective randomised study. J Arthroplasty. 2014 29(12):2373-7 DOI: 10.1016/j.arth.2013.12.010.
64. Kurmis AP. A role for artificial intelligence applications inside and outside of the operating theatre: a review of contemporary use associated with total knee arthroplasty. Arthroplasty. 2023 5(1):40 DOI: 10.1186/s42836-023-00189-0.
65. Stentz-Olesen K, Nielsen ET, De Raedt S, Jørgensen PB, Sørensen OG, Kaptein BL, et al. Validation of static and dynamic radiostereometric analysis of the knee joint using bone models from CT data. Bone Joint Res. 2017 6(6):376-384 DOI: 10.1302/2046-3758.66.Bjr-2016-0113.R3.
66. Hansen L, De Raedt S, Jorgensen PB, Mygind-Klavsen B, Kaptein B, Stilling M. Marker free model-based radiostereometric analysis for evaluation of hip joint kinematics: A validation study. Bone Joint Res. 2018 7(6):379-387 DOI: 10.1302/2046-3758.76.Bjr-2017-0268.R1.
67. Sandberg OH, Kärrholm J, Olivecrona H, Röhrl SM, Sköldenberg OG, Brodén C. Computed tomography-based radiostereometric analysis in orthopedic research: practical guidelines. Acta Orthop. 2023 94:373-378 DOI: 10.2340/17453674.2023.15337.
68. Engseth LHW, Schulz A, Pripp AH, Röhrl SMH, Øhrn FD. CT-based migration analysis is more precise than radiostereometric analysis for tibial implants: a phantom study on a porcine

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cadaver. Acta Orthop. 2023 94:207-214 DOI: 10.2340/17453674.2023.12306.
69. Broekhuis D, Boyle R, Karunaratne S, Chua A, Stalley P. Custom designed and 3D-printed titanium pelvic implants for acetabular reconstruction after tumour resection. Hip Int. 2022:11207000221135068 DOI: 10.1177/11207000221135068.
70. Choi HR, Bedair H. Mortality following revision total knee arthroplasty: a matched cohort study of septic versus aseptic revisions. J Arthroplasty. 2014 29(6):1216-8 DOI: 10.1016/j.arth.2013.11.026.
71. Roman MD, Russu O, Mohor C, Necula R, Boicean A, Todor A, et al. Outcomes in revision total knee arthroplasty (Review). Exp Ther Med. 2022 23(1):29 DOI: 10.3892/etm.2021.10951.
72. Ross RD, Deng Y, Fang R, Frisch NB, Jacobs JJ, Sumner DR. Discovery of biomarkers to identify peri-implant osteolysis before radiographic diagnosis. J Orthop Res. 2018 36(10):2754-2761 DOI: 10.1002/jor.24044.
73. Schoeman MA, Pijls BG, Oostlander AE, Keurentjes JC, Valstar ER, Nelissen RG, et al. Innate immune response and implant loosening: Interferon gamma is inversely associated with early migration of total knee prostheses. J Orthop Res. 2016 34(1):121-6 DOI: 10.1002/jor.22988.
74. de Poorter JJ, Hoeben RC, Hogendoorn S, Mautner V, Ellis J, Obermann WR, et al. Gene therapy and cement injection for restabilization of loosened hip prostheses. Hum Gene Ther. 2008 19(1):83-95 DOI: 10.1089/hum.2007.111.
75. Schilcher J, Palm L, Ivarsson I, Aspenberg P. Local bisphosphonate reduces migration and formation of radiolucent lines adjacent to cemented acetabular components. Bone Joint J. 2017 99-b(3):317-324 DOI: 10.1302/0301-620x.99b3.Bjj-2016-0531.R1.
76. Hilding M, Aspenberg P. Local peroperative treatment with a bisphosphonate improves the fixation of total knee prostheses: a randomized, double-blind radiostereometric study of 50 patients. Acta Orthop. 2007 78(6):795-9 DOI: 10.1080/17453670710014572.
77. Astrand J, Aspenberg P. Topical, single dose bisphosphonate treatment reduced bone resorption in a rat model for prosthetic loosening. J Orthop Res. 2004 22(2):244-9 DOI: 10.1016/j.orthres.2003.08.008.

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