



## Personalised medicine in knee arthroplasty: we need more science!

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In the last years, personalised medicine has been increasingly introduced in many medical fields. As early as in 2015, the European Union has released their council conclusions on personalised medicine for patients [13]. They stated that there is no commonly agreed definition of the term ‘personalised medicine’ [13]. However, it is widely understood that personalised medicine refers to a medical model using characterisation of individuals’ phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention.

In particular, in oncology and drug development, it has been identified as the biggest potential for further improvements [12]. For drug development, it is a fact that there are certain patients who benefit to a great extent from a drug treatment with limited or no side effects [12]. Some do benefit from the drugs, but suffer from side effects. Others do not benefit, but also have no side effects. Finally, others have no benefit, but show relevant side effects. What can be learned from this simple observation is that personalized medicine is worth looking into and in much more detail.

The pharmaceutical industry has understood that the high inter-individual variability in terms of anatomy and biological processes makes us more or less vulnerable for different diseases and pathologies, but also susceptible for specific treatments [6, 12].

When it comes to orthopaedics, personalised medicine has not really taken off yet. However, the basic circumstances are similar. Many medtech and health insurance companies as well registries are already collecting huge data about patients’ demographics, survival rates, revisions or outcomes such as PROMs [2]. A still neglected ‘treasure’ lies in planning or navigational data.

Over the last years we have identified patient populations with knee problems, who are more or less susceptible for good or bad outcomes and in many cases we do not understand why and do not have the optimal solutions. We have also seen patients who are more prone to suffer from a pathology such as osteoarthritis [1, 7]. Some call it the patient factor, and others call it optimal patient selection.

As Werner Müller, one of the godfathers of the modern European knee surgery once said, the only constant in anatomy is its variability [4]. However, when it comes to knee arthroplasty for the sake of material durability as well as simplification of instrumentation and manufacturing the pioneers of total knee arthroplasty (TKA) have made numerous assumptions, which for centuries have not been questioned as a whole. In the last years, the dogma that all knees should have a neutral hip-knee-ankle angle (HKA) after TKA has been questioned for native varus knees [11]. In addition, there is an ongoing discussion about the optimal alignment in TKA [3, 5, 8–10]. In fact, it appears that there is not only the mechanical alignment that matters, but there are more alignment options to be considered such as anatomic, kinematic and adjusted alignment [3, 5, 8–10].

Rather surprisingly we still have limited understanding of native and osteoarthritic knee alignment, but in spite of

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this, we already give systematic alignment recommendations [3, 5, 8–10]. There are only a few research studies dealing with the pertinent question what the native and osteoarthritic knee alignment is. Most of them are based on data of two-dimensional radiographs and are rather limited cohorts.

This issue of the journal contains a considerable number of studies and reviews dealing with native non-osteoarthritic knee alignment. These studies will help to obtain a better understanding of the inter-patient knee alignment variation.

A systematic review provides a necessary overview on current knowledge of native knee alignment [14].

In three landmark registry studies, knee alignment was measured in non-osteoarthritic knees using 3D-CT. The first deals with HKA, the second with joint line angles and the third provides a synopsis of all coronal alignment angles. Based on these data, the concept of ‘functional knee phenotypes’ is proposed. The knee can be classified based on alignment, laxity, morphology and physiology. The following classification of “Functional Knee Phenotypes” comprehensively characterizes all knee alignment information and proposes several knee phenotypes based on the findings of this study, which is based on non-osteoarthritic knees. These different phenotypes will add to a better understanding of knee function, and for each phenotype, an optimal functional and safe zone for alignment and TKA position needs to be identified.

It is important to note that the concept of personalized medicine in orthopaedics (Functional Knee Phenotype) goes way beyond than utilizing implants which are manufactured based on individual 3D-data (CT, MRI). This concept might help to structure and categorize the individual morphology and alignment between knees and help to identify the optimal TKA strategy in terms of alignment, bone cuts and grade of customization.

## References

1. Bowman EN, Hallock JD, Throckmorton TW, Azar FM (2018) Hyaluronic acid injections for osteoarthritis of the knee: predictors of successful treatment. *Int Orthop* 42(4):733–740
2. Hansen MM, Miron-Shatz T, Lau AY, Paton C (2014) Big data in science and healthcare: a review of recent literature and perspectives. *Contribution of the IMIA Social Media Working Group. Yearb Med Inform* 9:21–26
3. Hirschmann MT, Karlsson J, Becker R (2018) Hot topic: alignment in total knee arthroplasty—systematic versus more individualised alignment strategies. *Knee Surg Sports Traumatol Arthrosc* 26(6):1587–1588
4. Hirschmann MT, Muller W (2015) Complex function of the knee joint: the current understanding of the knee. *Knee Surg Sports Traumatol Arthrosc* 23(10):2780–2788
5. Jaffe WL, Dundon JM, Camus T (2018) Alignment and balance methods in total knee arthroplasty. *J Am Acad Orthop Surg* 26(20):709–716
6. Myin-Germeys I, Penninx B (2018) Personalised medicine: from a scientific perspective. *Tijdschr Psychiatr* 60(3):210–214
7. Raynauld JP, Martel-Pelletier J, Dorais M, Haraoui B, Choquette D, Abram F, Beaulieu A, Bessette L, Morin F, Wildi LM, Pelletier JP (2013) Total knee replacement as a knee osteoarthritis outcome: predictors derived from a 4-year long-term observation following a randomized clinical trial using chondroitin sulfate. *Cartilage* 4(3):219–226
8. Riviere C, Iranpour F, Auvinet E, Howell S, Vendittoli PA, Cobb J, Parratte S (2017) Alignment options for total knee arthroplasty: a systematic review. *Orthop Traumatol Surg Res* 103(7):1047–1056
9. Schiffner E, Wild M, Regenbrecht B, Schek A, Hakimi M, Thelen S, Jungbluth P, Schnependahl J (2018) Neutral or natural? Functional impact of the coronal alignment in total knee arthroplasty. *J Knee Surg*. <https://doi.org/10.1055/s-0038-1669788>
10. Slevin O, Hirschmann A, Schiapparelli FF, Amsler F, Huegler RW, Hirschmann MT (2018) Neutral alignment leads to higher knee society scores after total knee arthroplasty in preoperatively non-varus patients: a prospective clinical study using 3D-CT. *Knee Surg Sports Traumatol Arthrosc* 26(6):1602–1609
11. Slevin O, Hirschmann A, Schiapparelli FF, Amsler F, Huegler RW, Hirschmann MT (2017) Neutral alignment leads to higher knee society scores after total knee arthroplasty in preoperatively non-varus patients: a prospective clinical study using 3D-CT. *Knee Surg Sports Traumatol Arthrosc*. <https://doi.org/10.1007/s00167-017-4744-y>
12. van Vollenhoven RF, L’Ami M, Wolbink G (2018) Personalised medicine in rheumatology. *Tijdschr Psychiatr* 60(3):146–150
13. (2019) Council conclusions on personalised medicine for patients. [https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.C\\_.2015.421.01.0002.01.ENG%26toc=OJ:C%E2%80%992015%E2%80%99421%E2%80%99FULL](https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.C_.2015.421.01.0002.01.ENG%26toc=OJ:C%E2%80%992015%E2%80%99421%E2%80%99FULL)
14. Moser LB, Hess S, Amsler F, Behrend H, Hirschmann MT (2019) Native non-osteoarthritic knees have a highly variable coronal alignment—a systematic review. *Knee Surg Sports Traumatol Arthrosc*. <https://doi.org/10.1007/s00167-019-05417-2>

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