The Digital Twin Knee Value-Based Personalized Knee Care

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Introduction

Knee disorders are very common in patients of all ages. They vary from congenital disorders, trauma- & sports injuries to osteoarthritis. Osteoarthritis (OA) is the most common musculoskeletal disease.¹ OA is highly prevalent in the United States and around the globe.² It affects 1 in 3 people over age 65 and women more so than men (more than 32.5 million adults in the United States).² Almost half of these patients suffer from symptomatic knee OA (14 million people in the US in 2018).³ Notably, more than half of these patients were <65 years of age.³ In the Netherlands, 1.467.200 people were estimated to have OA in 2018.¹ The prevalence of OA is rising due to the increasing prevalence of OA risk factors such as obesity, physical inactivity, and joint injury.^{1, 2, 4-6}

OA is a leading cause of disability and negatively impacts patients' physical and mental well-being.^{1, 3} OArelated joint pain causes functional limitations, poor sleep, fatigue, depressed mood and loss of independence.³ Compared to age and sex-matched peers, OA patients incur higher out of pocket health-related expenditures and substantial costs due to lost productivity.² In a population-based study in Sweden, the greater risk for sick leave or disability among those working in female- or male-dominated job sectors was attributed to knee OA.³

Knee osteoarthritis & other medical conditions

Most people with OA (59-87%) have at least one other chronic condition, especially cardiometabolic conditions.² There is also increasing evidence that OA is a risk factor for cardiovascular disease development. A meta-analysis found that the risk of myocardial infarction was significantly increased in OA and other types of arthritis.^{3, 7} Other studies similarly linked coronary heart disease with OA.^{3, 8} In parallel, the Chingford Cohort study found an increased risk of cardiovascular disease-specific and all-cause mortality among women with symptomatic knee OA compared to women without signs or symptoms of OA.^{9, 10} Symptomatic knee OA may impair the ability of people with cardiometabolic conditions to exercise and lose weight, which is core to the management of these condition.^{1, 2} In longitudinal cohort studies, hip and knee OA is associated with higher risk for all-cause and cardiovascular death, largely due to OA-related difficulty walking.² Besides affecting people's physical health, OA may also negatively impact people's mental health. Data from the Osteoarthritis Initiative (OAI) study demonstrated that those with lower limb OA had greater odds of developing depressive symptoms than those without the disease.³ Another study found a strong relationship between OA and perceived memory loss that was partially mediated by sleep and mood impairment.³ Sleep disorders are common in patients with symptomatic knee OA as well as during the first 3 months post-surgery.¹

Patients with OA and other chronic conditions are less likely to receive a diagnosis and recommended treatment.¹ Furthermore, in these individuals the most effective and safest treatment is physical activity/exercise coupled with self-management strategies.¹⁻³ In practice however, this treatment strategy is poorly implemented.¹¹ A large regional network led by 17 orthopedic surgeons of Máxima Medical Center and Catharina Hospital (Orthopedie Groot Eindhoven) has recently started a large pilot "Zinnige Zorg" project with Insurance Company VGZ, PoZoB (association of general physicians Zuid-Oost Brabant) and 15 physiotherapy practices in the region of Eindhoven implementing a proven rehabilitation strategy from Denmark for knee and

^{4.} Eindhoven MedTech Innovation Center

hip OA patients (Good Life with Osteoarthritis Denmark = GLA:D B).^{11, 12} Given the already high and growing burden of OA, enhanced effort is required to identify better - more effective and safe - treatments for the majority of patients with OA who are living with other chronic conditions.^{2, 11}

Costs of knee osteoarthritis

Healthcare resources and costs associated with managing OA are substantial.^{1, 3, 4, 13} In fact, OA was the second most costly health condition treated at US hospitals in 2013. In that year, it accounted for \$16.5 billion, or 4.3%, of the combined costs for all hospitalizations. OA was also the most expensive condition for which privately insured patients were hospitalized, accounting for over \$6.2 billion in hospital costs.¹³ The economic burden due to OA is the result of direct costs to the health care system, indirect costs to individuals living with OA, and the intangible costs of living with a chronic disabling condition.¹³

Knee osteoarthritis & research

There is increasing evidence that there are different OA phenotypes that reflect different mechanisms of the disease. Various person-level risk factors are recognized, including sociodemographic characteristics (e.g. female sex, African-American race), genetic predispositions, obesity, diet-related factors, and high bone density/mass.^{1, 3} Joint-level risk factors include specific bone/joint shapes, thigh flexor muscle weakness, joint malalignment, participation in certain occupational/sports activities, and joint injury.^{1, 4, 6, 14-20} Recent studies have enhanced the understanding of pre-radiographic lesions associated with OA.^{3, 21} Application of new findings may allow to develop innovative strategies and novel therapies with the purpose of preventing onset of OA and minimizing OA progress.^{1, 3, 4, 16, 18, 20, 22-35}

The development of knee OA is multifactorial.¹ An important modifiable risk factor for knee OA is optimal treatment of knee injury.^{4, 5, 22} Injuries of the anterior cruciate ligament (ACL), meniscus, cartilage and other knee ligaments frequently occur in cutting and pivoting sports such as football, field hockey, indoor sports, alpine skiing and tennis.^{4-6, 16, 17} Surgical knee reconstructions techniques, diagnostic imaging techniques and rehabilitation have continually improved over the years.^{4, 15, 28, 36-38} Reconstructive orthopaedic surgery is the number 1 intervention that has the largest impact on sustained quality of life.³⁹ However, various clinical issues are still unresolved. Examples are re-injury rates of the ACL graft in both adult and pediatric ACL surgery (up to 30% in children), long-term OA after knee ligament surgery (54%), limited return to sports after ACL reconstruction (65%), and 20% patient dissatisfaction after total knee arthroplasty.^{1, 5, 6, 16, 17, 22, 25, 27, 31-34, 40-44} In addition, patient-related factors such as osseous morphology, gender, ACL graft type, type of sports, comorbidities, genetics, kinesophobia and rehabilitation influence patient outcome.^{4, 15, 20, 26, 28, 35-38, 45-48}

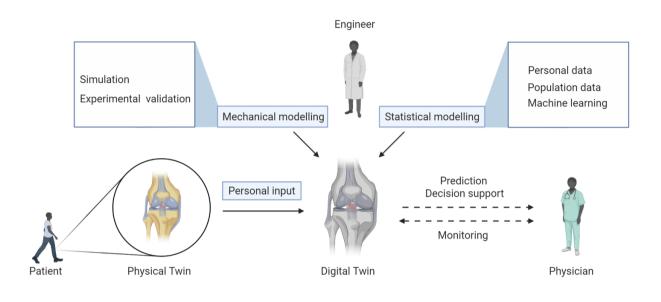
The human knee is a complex organ in structure and function.⁴ Prediction models, algorithms, shared decision programs and apps are being developed to improve patient stratification and prediction of outcome after treatment of knee disorders based on subjective and objective patient outcome, artificial intelligence and biomechanical tissue characteristics.^{14, 20, 24-27, 30, 33, 35, 43, 49-59} All these models add to the knowledge of knee reconstruction but do not embody all the necessary information for patient-specific decision making and optimal treatment outcome.

Digital Twin Knee

If physicians could use a scientific method to better understand and predict the outcome of a patient's condition, they could more effectively screen patients at hospitals and deliver personalized care.⁶⁰ Digital twins stand to revolutionize healthcare in the 21st century, paving the way to more personalized, preventive and participative treatment options that support a shift from reactive to proactive healthcare.^{60, 61} A digital twin (DT) is a digital replica of an object, process or system. They are used in design and to better understand how the system will behave over its lifecycle. The DT concept is already being used in product prognostics and product health management, as well as product design and manufacturing.^{62, 63} The DT of a product consists of combining a mechanical model (to understand and explain the physical state) and statistical models (to identify and predict patterns concerning the state). An important aspect is the connection between the physical object and the digital object, usually done by tracking markers in the physical state through sensors.^{64, 65} Aspects of the DT approach have been applied in health care, showing a great improvement in precision cardiology for example.⁶⁶ DT might be a cost-effective way to overcome limits in personalized healthcare. Recently development of a Digipredict DT has started to predict whether Covid-19 patients will develop severe cardiovascular complications and, in the long term, detect the likely onset of inflammatory disease. It makes use of data science and special biomarker detectors.⁶⁰

Primary goal of the *Digital Twin Knee* (*DT Knee*) is to provide a decision support for both patient and the treating physician to optimize value-based personalized knee care (*Fig. 1*).

Fig. 1. Concept of the Digital Twin Knee in practice

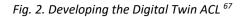


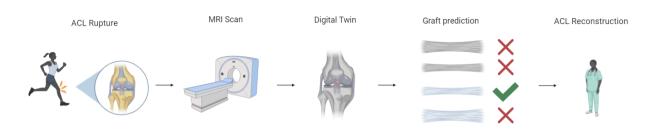
Concept of the digital twin in practice

Development of DT Knee will encompass translational research involving patients, engineers, data scientists, orthopedic surgeons, imaging experts and health care technology providers as well as legislation for privacy and data management. Research will focus on creating the DT of an injured knee. DT Knee serves to select the best type of knee treatment for each patient. It will allow patient-specific shared decision making between the patient and the physician as well as prediction of outcome considering all necessary subjective and objective parameters. Development of DT Knee can build upon current and future joint translational research between clinicians, TU/e engineers and major health care technology providers. It would incorporate current research lines at TU/e, Fontys University of Applied Sciences and Máxima Medical Center & Catharina Hospital on tissue level computer models to simulate damage accumulation in cartilage, biological platforms to evaluate tenocyte performance and clinical prediction models, surgical techniques, patient stratification, rehabilitation and valuebased health knee care (clinical outcome and costs) (Table 1,2). Furthermore, Orthopedie Groot Eindhoven/Máxima Medical Center is research partner in various PhD projects at Maastricht University, Radboud UMC Nijmegen, University of Leiden, AmsterdamUMC and Erasmus MC Rotterdam to accelerate valid data collection on prediction models, apps and treatment algorithms for knee disorders (Table 2). New joint research ventures are currently investigated with the Dept. of Electrical Engineering TU/e (prof.dr.ir. Cottaar; PDEng Clinical Informatics, PDEng Qualified Medical Engineer; SPME), Dept. of Mathematics and Computer Science TU/e (prof.dr. George Fletcher), Lectoraat Al&Big Data Fontys University of Applied Sciences (dr. Gerard Schouten), e/MTIC, Philips, Arthrex, VisualSonics, OnlinePROMS, Games for Health, BG. Legal (legislation for AI clinical data), TU Twente, Erasmus University, Utrecht University and Maastricht University (Table 2).

Recently, an NWO Demonstrator research project has started to explore the possibilities of the DT Knee

concept in graft selection for anterior cruciate ligament (ACL) reconstruction: *Developing the Digital Twin ACL* (Fig 2).⁶⁷





Several clinical issues in ACL reconstruction led to this project. Knee injuries and ACL rupture are important risk factors for development of knee OA.^{4, 35, 37, 38} Considering the increasing number of patients at (pre)-adolescent age with this type of injury, this will present a significant burden on patient well-being and cost of health care in the near future.^{4, 5, 16} There seems to be graft-specific risk for knee OA.³⁸ Monitoring capacities for the patient-specific healing process of the ACL graft after surgical reconstruction are limited.^{22, 46} Non-invasive assessment such as MRI imaging is available but is expensive, time consuming and cannot currently predict outcome.^{4, 28} Re-rupture risk of an ACL graft is age-dependent with various phenotypes.^{5, 45} With the annual increasing number of ACL reconstructive surgeries, a more effective way to monitor patient-specific graft choice and rehabilitation based on ACL graft remodeling is needed.^{4, 20, 22, 46, 47, 68}

The first step to create *DT ACL* is to build a virtual representation of the physical ACL itself and its environment.⁶⁶ This geometric and physical model will be made using FEA-software and validation will be done in the lab by mechanical experiments performed on human and animal ACLs. By developing this mechanical model, the foundation will be laid to further work towards a functional *DT ACL.*⁶⁷ Due to the importance of the connection between the physical model and the digital model, a method has to be developed to process data from the physical state that can be used in this mechanical mode.⁶³ As the DT approach also has its use as a design framework, the ACLs designed from the novel decellularization protocol from porcine tendons as well as human specimen ligament testing can be combined with the mechanical model to yield recommendations in design decision making for ACL reconstruction.^{69, 70} Current joint translational NWO Demonstrator / PhD research on tissue decellularization, biomarkers and photo-acoustic imaging for cartilage damage maps & human ACL graft remodeling contributes to this project (Dept. of Biomedical Engineering TU/e and Máxima Medical Center Eindhoven).^{20, 28, 47, 67, 70-72 68}

Digital Twin Knee & university curricula

DT Knee is incorporated in three university curricula.

Since 2019, 20 BSc students and a PhD candidate are working on patient expectations, experience, PROMs, outcome and costs in Value-Based Health Knee Care at Fontys University of Applied Sciences in cooperation with Orthopedie Groot Eindhoven (Máxima Medical Center & Catharina Hospital). The program is incorporated in the BSc Minor Personal Leadership in Value Based Collaborative Health Care (PLUSH). In February 2021, the first group of TU/e engineering students started on a proof of concept challenge for the *DT Knee*. This is initiated by TU/e Innovation Space Bachelor End Product for Honors Master Academy and challenge owner is Orthopedie Groot Eindhoven. This challenge on prediction models for knee reconstruction will involve engineers from various TU/e departments, designers, data scientists and physicians. Since February 2021, the new USE LL (User, Society and Entrepreneurial Learning line) *Digital Twin Health* at TU/e will further enhance continuity in developing *DT Knee & DT ACL* submodel for value-based personalized

knee care. From Sept 2021, 10 students will annually participate in the learning line Digital Twin Knee focusing

on patient remote monitoring through sensor/brace technology in daily and sports activities.

The future

Essential for *DT Health* is reliable clinical & research data in interconnected health information systems.⁷³ *DT Knee* & *DT ACL* require enhancement of knee scale finite models, biological platforms for cartilage and tissue remodeling and enhanced diagnostics (e.g. motion-biosensors, arthrometry systems for joint instability, biomarkers and (non)-invasive dynamic imaging techniques). In addition, patient remote monitoring would

allow diagnosis in real life situations when the patient experiences the specific complaints. Remote patient management will allow for better value-based knee care by new transmural health care models as well as reduction of hospital visits and hospital stay. Holistic tracking of ADL/sports activities will also help to personalize rehabilitation for each patient feeding their *DT Knee* with personalized data.⁷³ Smart analytics in AI & Big Data need to be developed for personalized prediction and decision support.⁷³ This also applies to the necessary legal and ethical issues for use of AI and large-scale personalized clinical data in *DT Health*. Block chain technology may have the potential to transform health care, placing the patient at the center of the health care ecosystem and increasing the security, privacy, and interoperability of health data.⁷³ Furthermore, the relationship between knee OA, cardiovascular and sleep disorders offers opportunities for joint research on a larger scale by clinicians, TU/e engineers and health care technology providers. *DT Knee* offers elaborate translational research possibilities on materials for regenerative medicine, diagnosis & surgical reconstruction techniques and profound analysis of the pathologies in the complex structural system of the knee. The current translational research, education, strong clinical relationship and (inter)national network form a solid basis for cooperation with new partners and stakeholders in the future.

Table 1. Current contributors Digital Twin Knee Eindhoven

Máxima MC/STZ Center of Expertise Complex Knee injuries/European Research Center Pediatric ACL injuries (Chair dr. Rob Janssen MD)

- 2 Senior researchers (dr. Marieke van der Steen, dr. Wai-Yan Liu)
- 1 Research assistant (Tessa van de Kerkhof BSc)
- 2 PhD candidates (Martijn Dietvorst MD, Sander van Eijck MD)
- 2 MSc students Maastricht University (Ninne Mille BSc, Daan Janssen BSc)

Orthopedie Groot Eindhoven (Dept. of Orthopaedic Surgery & Trauma, Máxima MC & Catharina Hospital)

8 Orthopaedic surgeons (Marijn van den Besselaar MD, Willem den Boer MD, Janneke Bos MD, dr. Hans Hendriks MD, dr. RPA Janssen MD, Coen Jaspars MD, Robin van Kempen MD, Remco van Wensen MD)

Value-Based Health Care, Faculty of Paramedical Sciences, Fontys University of Applied Sciences (Chair dr. Rob Janssen MD, lector)

2 Senior researchers (dr. Mitchel van Eeden, dr. Madelon Pijnenburg)

- 12 Lecturer-researchers (Team Interprofessioneel Samenwerken)
- 1 PhD candidate (Anouk Konings-Pijnappels MSc)

43 BSc students in 5 research lines on value-based health care (since Sept. 2019)

AI & Big Data, Faculty of ICT, Fontys University of Applied Sciences (Chair dr.ir. Gerard Schouten, lector)

1 Senior lecturer – project leader AI & Big Data (Michiel Groenemeijer MSc)

1 Senior researcher-lecturer (dr.ir. Simona Orzan)

High tech Embedded Software, Faculty of ICT, Fontys University of Applied Sciences (Chair dr.ir. Taede Punter, lector)

Orthopaedic Biomechanics, Dept. of Biomedical Engineering, TU/e (Chair prof.dr. Keita Ito)

2 Associate professors (dr. René van Donkelaar, dr. Rob Janssen MD)

2 Assistant professors (dr.ir. Jasper Foolen, dr.ir. Wouter Wilson)

3 PhD candidates (Marc van Vijven MSc, Meike Kleuskens MSc, Janne Spierings MSc)

5 MSc students (Despina Stefanoska, Joyce Kimenai, Meike Boef, Pieter Zwerver, Wietske Velthuis)

BioInterface Science, Dept. of Biomedical Engineering, TU/e (Chair prof.dr. Jan de Boer)

- 1 Postdoc (dr. Jorge Uquillas Paredes)
- 1 PhD candidate (Aysegul Dede-Eren MSc)
- 3 MSc students (Janne Spierings, Marloes van den Hengel, Antonio van der Lande)

Cardiovascular Biomechanics, Dept. of Biomedical Engineering / e/MTIC (dr.ir. Richard Lopata) 1 Assistant professor (dr. Min Wu)

School of Medical Physics and Engineering, Dept. of Electrical Engineering, TU/e (Chair prof.dr. Ward Cottaar) 1 annual PDEng Clinical Informatics and PDEng Qualified Medical Engineer

Database Group, Data and Artificial Intelligence Cluster. Dept. of Mathematics and Computer Science, TU/e (chair prof.dr. George Fletcher)

Innovation Space Bachelor End Project for Honors Masters Academy, TU/e

1. Challenge owner (dr. Rob Janssen MD)

3 Academic coaches (prof.dr. George Fletcher, dr. Jasper Foolen, dr. Peter Ruijten-Dodoiu)

1 MSc student (Kim Geelink, BSc)

3 BSc students TU/e (Jovan Sakovic Datascience, Délano Gaasbeek Psychology&Technology, Kelly Morrenhof BME)

USE LL (User, Society and Entrepreneurial Learning line) Digital Twin Anterior Cruciate Ligament

1 Professor (prof.dr. Jan de Boer, coordinator)

1 Associate professor (dr. Rob Janssen MD)

2 Assistant professors (dr.ir. Jasper Foolen, dr. Burcu Gumuscu)

1 Postdoc (dr. Jorge Uquillas Paredes)

1 PhD candidate (Sander van Eijck, MD)

2 MSc student (Kim Geelink BSc, Antonio van der Lande BSc)

4 BSc students TU/e – UMCU (K. Morrenhof, D. Brink BME, T. Haning Med Wet & Tech, L. Vlootman Psych & Tech, R. Ganesh Med) 25 annual BSc students TU/e from September 2021 in Digital Twin Health Program

Table 2. Subprojects

Current and finished projects and related publications (principal investigator)

Name	Goal	Partners	Funding
ACL reconstruction & accelerated rehabilitation in adult and pediatric patients ⁴⁻ 6, 15-17, 22, 26, 35-38, 40, 42, 45, 46, 50-52, 55, 57	Optimal treatment conservative vs surgical reconstruction & rehabilitation: outcome, return to play, osteoarthritis, remodelling, complications and PROMs. (3 national guidelines on rehabilitation)	MMC, OGE, UM, Aarhus University (DK), Charité (Berlin DE), NVA, FMS, NOV, KNGF, ESSKA	Dept. Orthopaedics MMC (2 PhD's)
Knee & hip osteoarthritis ^{14, 18,} 19, 27, 29, 31-34, 41, 43, 53, 54, 56, 74	Patient expectations & satisfaction, outcome, prediction models in knee and hip surgery and physiotherapeutic treat-to-target rehabilitation after orthopaedic surgery	MMC, ErasmusMC, NOV-LROI, OGE, Fontys	Dept. Orthopaedics MMC NOV (1 PhD)
Remodelling ACL grafts and rehabilitation in adult and pediatric patients ^{16, 20, 22, 28, 46, 47, 67, 68, 70-72, 75}	Development of a decellularized ACL allograft & tissue platform for predic- ting graft remodeling and rehabilitation strategies	MMC, TU/e (BME: OB & BS; IS, USE LL), OGE, UMCU, BisLife, MUMC+, OCON, StAntoniusZH, StAnna, PSV	Dept. Orthopaedics MMC TU/e, NWO (2 PhD's, 1 postdoc)
Knee reconstruction and cartilage degeneration ²³	To develop and evaluate an ex-vivo human osteochondral culture model	TU/e (BME: OB), MMC, OGE, UMCU	TU/e (1 PhD)

Current multicenter projects and related publications (MMC participating center)

Name	Goal	Partners	Funding
ROTATE trial ⁷⁶	To compare a new algorithm to usual	ErasmusMC, MMC, MartiniZH,	ZonMW
	shared-decision making for treatment	StAntoniusZH, TergooiZH, Noord-	(1 PhD)
	strategies in ACL injured patients	westZH groep, HaaglandenMC	
STARR trial ⁷⁷	To compare arthroscopic resection vs.	ErasmusMC, MMC, CZE,	ZonMW
	rehabilitation in traumatic meniscal	HaaglandenMC, StAntoniusZH,	(1 PhD)
	injury		
Personalized m/eHealth	To analyze cost-effectiveness of a	AmsterdamUMC, MMC, Amphia,	ZonMW
Algorithm for the Resump-	transmural integrated care program for	MUMC+	(1 PhD)
tion of Activities of Daily Life,	knee arthroplasty patients in the		
Work and Sport after knee	working population		
arthroplasty ^{25, 59}			
CREDO ²¹	Developing and validating diagnostic	ErasmusMC, MMC, LUMC,	ZonMW
	criteria for early hip & knee OA	AmsterdamUMC, UMCU	(1 PhD)
Patient empowerment	App development for personalized	RadboudUMC, MMC, OGE,	RadboudUMC,
through timely information ⁴⁹	rehabilitation in orthopaedic medicine	OnlinePROMS, ViecuriMC, StAnna,	OnlinePROMS
		ViaSana	external PhD (1)
"Choosing Wisely"	Implementation of cost-effective	LUMC, MMC, UMCG	ZonWM
recommendations in	treatments and rehabilitation in		(1 PhD)
degenerative knee disease ^{58,} ^{78 79}	patients with degenerative knee disease		

Planned projects and related publications

Name	Goal	Partners	Funding
Remote patient	To develop value-based digital	OGE, MMC, CZE, TU/e (IS, SMPE, ID,	Dept. Orthopaedics
management / EHealth in	strategies for remote patient manage-	USE LL), UM, OnlinePROMS, B.G.	MMC, OGE
orthopaedic surgery ⁸⁰	ment in diagnosis & rehabilitation	Legal. Fontys. PSV? e/MTIC?	(1 PhD), 1PDEng
		Philips?	QMEPDEng
Good Life with Osteoarthritis	Transmural value-based health care for	OGE, MMC, VGZ Zinnige zorg,	OGE, MMC, Fontys,
NL ^{12, 74} (n=521, April 2021)	knee and hip osteoarthritis (outcome,	Fontys, PoZoB, regional network 15	VGZ. Application

	costs, bundled payments). Pilot to be	physioherapist practices, University	currently being
			, ,
	followed by national implementation NL	South Denmark (DK). LUMC?	written (1 PhD)
Digital Twin Knee ⁸¹⁻⁸³	Mainframe for value-based	OGE, MMC, CZE, TU/e (BME: OB, IS,	Dept. Orthopaedics
	personalized knee care. Blueprint can	CB; IS; USE LL; SMPE), TUTwente,	MMC, OGE, TU/e
	be translated to other fields of	ErasmusMC, OnlinePROMS, Games	(3 PhD's). Further
	orthopaedics and medicine	for Health, RadboudUMC. Fontys,	options are
		NOV, PSV. Philips? e/MTIC?	currently explored
Imaging of knee for	To develop new (non-)invasive tech-	OGE, MMC, TU/e (BME: OB, BS, CB;	Applications
biomechanics, cartilage,	niques in ultrasound and photoacoustic	USE LL), UMCU. Arthrex,	currently being
meniscus and remodeling	imaging for personalized rehabilitation	VisualSonics. Philips? e/MTIC?	written (2 PhD's)
ACL ^{29, 34}			
Rehabilitation in pediatric	Develop value-based strategies for	OGE, MMC, StAnna, KNGF, PSV,	Dept. Orthopaedics
ACL injured patients	personalized rehabilitation in children	NVA, ESSKA, PAMI. e/MTIC?	MMC, StAnna, NVA
			(1 Postdoc, 1 PhD)
Data platform orthopaedic	To define a data/application structure	OGE, MMC, TU/e, NOV, Fontys.	Dept. Orthopaedics
medicine	for a health platform to relate all	e/MTIC? Philips?	MMC, Fontys, TU/e
	current orthopaedic/radiology systems		(SPME) (1 PDEng, 1
			postdoc)
Biofeedback technology for	To develop a hometraining easy to use	OGE, MMC, TU/e (ID), Fontys.	TU/e (ID) (1 MSc),
personalized rehabilitation	biofeedback tool to stimulate	e/MTIC? Philips?	1PDEng QME
	quadriceps training with gamification		-

Abbreviations:

MMC Máxima Medical Center Eindhoven

OGE Orthopedie Groot Eindhoven

UM Universiteit Maastricht

NVA Nederlandse Vereniging voor Arthroscopie

FMS Federatie Medisch Specialisten

NOV-LROI Nederlandse Orthopaedische Vereniging – Landelijke Registratie Orthopedische Implantaten

KNGF Koninklijk Nederlands Genootschap voor Fysiotherapie

ESSKA European Society for Sports Traumatology, Knee Surgery and Arthroscopy

PAMI Pediatric Anterior cruciate ligament Monitoring Initiative

BME Dept. of Biomedical Engineering, TU/e

OB, BS, CB Orthopaedic Biomechanics, BioInterface Science, Cardiovascular Biomechanics (BME, TU/e)

IS; USE LL InnovationSpace; User, Society and Entrepreneurial Learning line (students from all departments TU/e)

SMPE School of Medical Physics and Engineering (PDEng Clinical Informatics), Dept. of Electrical Engineering, TU/e

ID Industrial Design, Dept. of Electrical Engineering, TU/e

UMCU Universitair Medisch Centrum Utrecht

MUMC+ Maastricht Universitair Medisch Centrum

OCON Orthopedisch Centrum Oost Nederland

CZE Catharina Ziekenhuis Eindhoven

LUMC Leids Universitair Medisch Centrum

UMCG Universitair Medisch Centrum Groningen

PoZoB Praktijk ondersteuning Zuid-oost Brabant

e/MTIC Eindhoven MedTech Innovation Center

References

1. Tolk JJ (2020) Expectations and Outcome in Knee & Hip Arthroplasty PhD, *Erasmus University Rotterdam, The Netherlands*

2. Hawker GA (2019) Osteoarthritis Is a Serious Disease. Clin Exp Rheumatol 37 Suppl 120(5):3-6

- 3. Vina ER, Kwoh CK (2018) Epidemiology of Osteoarthritis: Literature Update. *Curr Opin Rheumatol* 30(2):160-167
- 4. Janssen RPA (2016) Anterior Cruciate Ligament & Accelerated Rehabilitation. Hamstring Tendons, Remodeling and Osteoarthritis. PhD, *Maastricht University, The Netherlands*
- Dietvorst M, Reijman M, van Zutven R, van den Bekerom MPJ, Meuffels DE, Somford MP, Janssen RPA (2021) Current State of Care for Pediatric Acl Ruptures in the Netherlands: A Survey. J Knee Surg 34(05):520-525
- Janssen RPA, van Mourik JBA (2019) Knieletsels Bij Kinderen. In: Kramer WLM, et al. (eds) Kindertraumachirurgie, 2nd. 2nd edn. Bohn Stafleu van Loghum, Imprint of Springer Nature, Houten, The Netherlands, pp 617-633

- 7. Schieir O, Tosevski C, Glazier RH, Hogg-Johnson S, Badley EM (2017) Incident Myocardial Infarction Associated with Major Types of Arthritis in the General Population: A Systematic Review and Meta-Analysis. *Ann Rheum Dis* 76(8):1396-1404
- 8. Chung WS, Lin HH, Ho FM, Lai CL, Chao CL (2016) Risks of Acute Coronary Syndrome in Patients with Osteoarthritis: A Nationwide Population-Based Cohort Study. *Clin Rheumatol* 35(11):2807-2813
- 9. Kluzek S, Sanchez-Santos MT, Leyland KM, Judge A, Newton J, Arden NK (2016) Response To: 'Painful Knee but Not Hand Osteoarthritis Is an Independent Predictor of Mortality over 23 Years Follow-up of a Population-Based Cohort of Middle-Aged Women' by Gao Et Al. *Ann Rheum Dis* 75(4):e23
- Kluzek S, Sanchez-Santos MT, Leyland KM, Judge A, Spector TD, Hart D, Cooper C, Newton J, Arden NK (2016) Painful Knee but Not Hand Osteoarthritis Is an Independent Predictor of Mortality over 23 Years Follow-up of a Population-Based Cohort of Middle-Aged Women. *Ann Rheum Dis* 75(10):1749-1756
- 11. Skou ST, Roos EM (2017) Good Life with Osteoarthritis in Denmark (Gla:D): Evidence-Based Education and Supervised Neuromuscular Exercise Delivered by Certified Physiotherapists Nationwide. *BMC Musculoskelet Disord* 18(1):72
- 12. Nolles J (2020) Deense Behandelwijze Voor Artrosepatiënten: Snel Minder Pijn in Knieën En Heupen. *Eindhovens dagblad* October 10 <u>https://www.ed.nl/veldhoven/deense-behandelwijze-voor-artrosepatienten-snel-minder-pijn-in-knieen-en-heupen~ad3bfbfc/</u>
- 13. Cdc Centers for Disease Control and Prevention. The Cost of Arthritis in Us Adults. (2020). https://www.cdc.gov/arthritis/data_statistics/cost.htm. Accessed February 21 2021
- 14. de Kroon KE, Houterman S, Janssen RPA (2012) Leg Alignment and Tibial Slope after Minimal Invasive Total Knee Arthroplasty: A Prospective, Randomized Radiological Study of Intramedullary Versus Extramedullary Tibial Instrumentation. *Knee* 19(4):270-274
- 15. Engelen-van Melick N, Brooijmans FAM, Janssen RPA (2014) Revalidatie Na Voorste-Kruisbandreconstructie. Bohn Stafleu van Loghum, Imprint of Springer Media, Houten, The Netherlands
- 16. Janssen RPA, Lind M, Engebretsen L, Moksnes H, Seil R, Fauno P, Murray M (2018) Pediatric Acl Injuries: Treatment and Challenges. In: Kerkhoffs GMMJ, et al. (eds) *Esska Instructional Course Lecture Book: Glasgow 2018*. Springer, Berlin, Germany, pp 241-259
- 17. Meuffels DE, Diercks RL, Hoogeslag R, Brouwer RW, Janssen RPA, Leenhouts PA, Goedhart EA, Lenssen AF (2018) Richtlijn Voorste Kruisbandletsel. *Richtlijnen database, Federatie Medisch Specialisten*,
- 18. Tolk JJ, Koot HW, Janssen RPA (2012) Computer Navigated Versus Conventional Total Knee Arthroplasty. *J Knee Surg* 25(4):347-352
- 19. van Groningen B, den Teuling JW, Houterman S, Janssen RPA (2015) Femoral Mechanical-Anatomical Angle Measurements in Total Knee Arthroplasty: Analog Versus Digital. *J Knee Surg* 28(4):315-319
- 20. van Vijven M, van Groningen B, Kimenai JN, van der Steen MC, van Doeselaar M, Janssen RPA, Ito K, Foolen J (2020) Identifying Potential Patient-Specific Predictors for Anterior Cruciate Ligament Reconstruction Outcome - a Diagnostic in Vitro Tissue Remodeling Platform. *J Exp Orthop* 7(1):48
- 21. Wang Q, Runhaar J, Kloppenburg M, Boers M, Bijlsma JWJ, Bierma-Zeinstra SMA, Credo EG (2020) The Added Value of Radiographs in Diagnosing Knee Osteoarthritis Is Similar for General Practitioners and Secondary Care Physicians; Data from the Check Early Osteoarthritis Cohort. J Clin Med 9(10):3374
- 22. Janssen RPA, Scheffler SU (2018) Graft Remodeling & Ligamentization after Acl Reconstruction. In: Prodromos CC (ed) *The Anterior Cruciate Ligament: Reconstruction and Basic Science* 2nd. 2nd edn. Saunders, an imprint of Elsevier, Inc, Philadelphia, USA, pp 342-347
- 23. Kleuskens MWA, van Donkelaar CC, Kock LM, Janssen RPA, Ito K (2021) An Ex Vivo Human Osteochondral Culture Model. *J Orthop Res* 39(4):871-879
- 24. Naghibi H, Janssen D, Van Tienen T, Van de Groes S, Van de Boogaard T, Verdonschot N (2020) A Novel Approach for Optimal Graft Positioning and Tensioning in Anterior Cruciate Ligament Reconstructive Surgery Based on the Finite Element Modeling Technique. *Knee* 27(2):384-396
- 25. Straat AC, Coenen P, Smit DJM, Hulsegge G, Bouwsma EVA, Huirne JAF, van Geenen RC, Janssen RPA, Boymans T, Kerkhoffs G, Anema JR, Kuijer P (2020) Development of a Personalized M/Ehealth Algorithm for the Resumption of Activities of Daily Life Including Work and Sport after Total and Unicompartmental Knee Arthroplasty: A Multidisciplinary Delphi Study. *Int J Environ Res Public Health* 17(14)
- 26. Theunissen WWES, van der Steen MC, Liu WY, Janssen RPA (2020) Timing of Anterior Cruciate Ligament Reconstruction and Preoperative Pain Are Important Predictors for Postoperative Kinesiophobia. *Knee Surg Sports Traumatol Arthrosc* 28(8):2502-2510

- 27. Tolk JJ, Waarsing JEH, Janssen RPA, van Steenbergen LN, Bierma-Zeinstra SMA, Reijman M (2020) Development of Preoperative Prediction Models for Pain and Functional Outcome after Total Knee Arthroplasty Using the Dutch Arthroplasty Register Data. J Arthroplasty 35(3):690-698 e692
- 28. van Groningen B, van der Steen MC, Janssen DM, van Rhijn LW, van der Linden AN, Janssen RPA (2020) Assessment of Graft Maturity after Anterior Cruciate Ligament Reconstruction Using Autografts: A Systematic Review of Biopsy and Magnetic Resonance Imaging Studies. Arthrosc Sports Med Rehabil 2(4):e377-e388
- 29. Wu M, van Teeffelen B, Ito K, van de Vosse FN, Janssen RPA, van Donkelaar CC, Lopata RGP (2021) Spectroscopic Photoacoustic Imaging of Cartilage Damage. *Osteoarthritis and Cartilage*,
- 30. Groot L, Gademan MGJ, Peter WF, van den Hout WB, Verburg H, Vliet Vlieland TPM, Reijman M, Pa TIOsg (2020) Rationale and Design of the Patio Study: Physiotherapeutic Treat-to-Target Intervention after Orthopaedic Surgery. *BMC Musculoskelet Disord* 21(1):544
- 31. Tolk JJ, Janssen RPA, Haanstra TM, Bierma-Zeinstra SMA, Reijman M (2018) The Ekspect Study: The Influence of Expectation Modification in Knee Arthroplasty on Satisfaction of Patients: Study Protocol for a Randomized Controlled Trial. *Trials* 19(1):437
- 32. Tolk JJ, Janssen RPA, Haanstra TM, van der Steen MC, Bierma-Zeinstra SMA, Reijman M (2020) The Influence of Expectation Modification in Knee Arthroplasty on Satisfaction of Patients: A Randomized Controlled Trial: The Ekspect Study. *The Bone & Joint Journal (accepted for publication November 20, 2020)*,
- 33. Tolk JJ, Janssen RPA, Haanstra TM, van der Steen MMC, Bierma Zeinstra SMA, Reijman M (2020) Outcome Expectations of Total Knee Arthroplasty Patients: The Influence of Demographic Factors, Pain, Personality Traits, Physical and Psychological Status. *J Knee Surg* 33(10):1034-1040
- 34. Brinkhof S, Froeling M, Janssen RPA, Ito K, Klomp DWJ (2020) Can Sodium Mri Be Used as a Method for Mapping of Cartilage Stiffness? *MAGMA*, 2020/11/13, 10.1007/s10334-020-00893-x
- 35. Janssen RPA, du Mee AW, van Valkenburg J, Sala HA, Tseng CM (2013) Anterior Cruciate Ligament Reconstruction with 4-Strand Hamstring Autograft and Accelerated Rehabilitation: A 10-Year Prospective Study on Clinical Results, Knee Osteoarthritis and Its Predictors. *Knee Surg Sports Traumatol Arthrosc* 21(9):1977-1988
- 36. Brooijmans FAM, Lenssen AF, Engelen-van Melick N, Knoop J, Rondhuis G, Neeleman-van der Steen CWM, Rtak IJR, Hullegie W, Hendriks HJM, Janssen RPA (2015) Evidence Statement Acuut Knieletsel. *KNGF*,
- 37. Janssen RPA, van Melick N, van Mourik JBA, Reijman M, van Rhijn LW (2018) Acl Reconstruction with Hamstring Tendon Autograft and Accelerated Brace-Free Rehabilitation: A Systematic Review of Clinical Outcomes. *BMJ Open Sport Exerc Med* 4(1):e000301
- 38. Janssen RPA, Van Melick N, van Mourik JBA, Reijman M, van Rhijn LW (2017) Similar Clinical Outcome between Patellar Tendon and Hamstring Tendon Autograft after Anterior Cruciate Ligament Reconstruction with Accelerated, Brace-Free Rehabilitation: A Systematic Review. *Journal of ISAKOS: Joint Disorders & Orthopaedic Sports Medicine* 2:308-317
- 39. Levi M (2021) Keynote Lecture: De Pandemie, En Dan.... *Paper presented at the NOV symposium & ALV 2021*, Webinar, February 4
- 40. Dietvorst M, Brzoskowski MH, van der Steen M, Delvaux E, Janssen RPA, Van Melick N (2020) Limited Evidence for Return to Sport Testing after Acl Reconstruction in Children and Adolescents under 16 Years: A Scoping Review. *J Exp Orthop* 7(1):83
- 41. Fuchs MC, Janssen RPA (2015) Clinical Evaluation of 292 Genesis Ii Posterior Stabilized High-Flexion Total Knee Arthroplasty: Range of Motion and Predictors. *Eur J Orthop Surg Traumatol* 25(1):161-166
- 42. Janssen RPA, Reijman M, Janssen DM, van Mourik JB (2016) Arterial Complications, Venous Thromboembolism and Deep Venous Thrombosis Prophylaxis after Anterior Cruciate Ligament Reconstruction: A Systematic Review. *World J Orthop* 7(9):604-617
- 43. Tolk JJ, van der Steen MC, Janssen RPA, Reijman M (2017) Total Knee Arthroplasty: What to Expect? A Survey of the Members of the Dutch Knee Society on Long-Term Recovery after Total Knee Arthroplasty. J Knee Surg 30(6):612-616
- 44. van Dijk WA, van Eerten PV, Janssen RPA, Roumen RMH, Scheltinga MRM (2017) Chronic Neuralgia after Knee Surgery. *Ned Tijdschr Geneeskd* 161:D2084
- 45. Dietvorst M, Verhagen S, van der Steen MC, Fauno P, Janssen RPA (2021) Lateral Tibiofemoral Morphometry Does Not Identify Risk of Re-Rupture after Acl Reconstruction in Children and Adolescents. *Knee Surg Sports Traumatol Arthrosc (under review)*,

- 46. Janssen RPA, Scheffler SU (2014) Remodeling of Hamstring Tendon Grafts after Acl Reconstruction. In: Siebold R, et al. (eds) *Anterior Cruciate Ligament Reconstruction: A Practical Surgical Guide*. Springer, Heidelberg, Germany, pp 257-265
- 47. van Vijven M, van Groningen B, Janssen RPA, van der Steen MC, van Doeselaar M, Stefanoska D, Ito K, Foolen J (2021) Local Variations in Mechanical Proporties of Human Hamstring Tendons Do Not Result in Mechanical Inferiority of One Particular Strand within an Autograft for Anterior Cruciate Ligament Reconstruction. *Journal of the Biomechanical Behavior of Biomaterials (under review)*,
- 48. van Melick N (2019) Return to Play after Anterior Cruciate Ligament Reconstruction in Pivoting Athletes. It's Time to Reconstruct Rehabilitation. PhD, *Radboud University Nijmegen, The Netherlands*
- 49. Timmers T (2021) Patient Empowerment through Timely Information. PhD, *Radboud University Nijmegen, The Netherlands*
- 50. Dietvorst M, Reijman M, van Groningen B, van der Steen MC, Janssen RPA (2019) Proms in Paediatric Knee Ligament Injury: Use the Pedi-Ikdc and Avoid Using Adult Proms. *Knee Surg Sports Traumatol Arthrosc* 27(6):1965-1973
- 51. Janssen RPA, van der Velden MJ, Pasmans HL, Sala HA (2013) Regeneration of Hamstring Tendons after Anterior Cruciate Ligament Reconstruction. *Knee Surg Sports Traumatol Arthrosc* 21(4):898-905
- 52. Janssen RPA, van der Velden MJF, van den Besselaar M, Reijman M (2017) Prediction of Length and Diameter of Hamstring Tendon Autografts for Knee Ligament Surgery in Caucasians. *Knee Surg Sports Traumatol Arthrosc* 25(4):1199-1204
- Tolk JJ, Janssen RPA, Prinsen C, van der Steen MMC, Bierma Zeinstra SMA, Reijman M (2019)
 Measurement Properties of the Oarsi Core Set of Performance-Based Measures for Hip Osteoarthritis:
 A Prospective Cohort Study on Reliability, Construct Validity and Responsiveness in 90 Hip Osteo-Arthritis Patients. Acta Orthop 90(1):15-20
- 54. Tolk JJ, Janssen RPA, Prinsen CAC, Latijnhouwers D, van der Steen MC, Bierma-Zeinstra SMA, Reijman M (2019) The Oarsi Core Set of Performance-Based Measures for Knee Osteoarthritis Is Reliable but Not Valid and Responsive. *Knee Surg Sports Traumatol Arthrosc* 27(9):2898-2909
- 55. van der Heijden LLM, Reijman M, van der Steen MCM, Janssen RPA, Tuijthof GJM (2019) Validation of Simendo Knee Arthroscopy Virtual Reality Simulator. *Arthroscopy* 35(8):2385-2390
- 56. van der Velden CA, Tolk JJ, Janssen RPA, Reijman M (2017) When Is It Safe to Resume Driving after Total Hip and Total Knee Arthroplasty? A Meta-Analysis of Literature on Post-Operative Brake Reaction Times. *Bone Joint J* 99-B(5):566-576
- 57. van der Velden CA, van der Steen MC, Leenders J, van Douveren F, Janssen RPA, Reijman M (2019) Pedi-Ikdc or Koos-Child: Which Questionnaire Should Be Used in Children with Knee Disorders? *BMC Musculoskelet Disord* 20(1):240
- 58. Rietbergen T, Diercks RL, Anker-van der Wel I, van den Akker-van Marle ME, Lopuhaa N, Janssen RPA, van der Linden-van der Zwaag HMJ, Nelissen R, Marang-van de Mheen PJ, van Bodegom-Vos L (2020) Preferences and Beliefs of Dutch Orthopaedic Surgeons and Patients Reduce the Implementation of "Choosing Wisely" Recommendations in Degenerative Knee Disease. Knee Surg Sports Traumatol Arthrosc 28(10):3101-3117
- 59. Straat AC, Coenen P, Kuijer P, Janssen RPA, Liu WY, Anema JR (2020-) (Cost-)Effectiveness of a Transmural Integrated Care Program for Knee ArthropIsty Patients in the Working Population (the Active Trial).
- Geneux V (2020) Digipredict Digital Twin Will Predict the Evolution of Covid-19. <u>https://actu.epfl.ch/news/digipredict-digital-twin-will-predict-the-evolutio/</u>. Accessed February 13
 2021
- 61. Philips Digital Twin Concept. (2018). <u>https://youtu.be/H6JzPCbyVSM</u>.
- 62. Tao F, Liu A, Hu T, Nee A (2019) Digital Twin Driven Smart Design. Elsevier,
- 63. Tao F, Sui F, Liu A, al. e (2019) Digital Twin-Driven Product Design Framework. *International Journal of Production Research* 57(12):3935-3953
- 64. Pires F, Cachada A, Barbosa J, Moreira AP, Leitao P (2019) Digital Twin in Industry 4.0: Technologies, Applications and Challenges. *Paper presented at the IEEE International Conference on Industrial Informatics (INDIN)*, Helsinki, Finland, July 22-25
- 65. Adi Otosense Smart Motor Sensor (Sms). <u>https://vimeo.com/509899366</u>. Accessed February 14 2021
- 66. Corral-Acero J, Margara F, Marciniak M, Rodero C, Loncaric F, Feng Y, Gilbert A, Fernandes JF, Bukhari HA, Wajdan A, Martinez MV, Santos MS, Shamohammdi M, Luo H, Westphal P, Leeson P, DiAchille P, Gurev V, Mayr M, Geris L, Pathmanathan P, Morrison T, Cornelussen R, Prinzen F, Delhaas T, Doltra A, Sitges M, Vigmond EJ, Zacur E, Grau V, Rodriguez B, Remme EW, Niederer S, Mortier P, McLeod K,

Potse M, Pueyo E, Bueno-Orovio A, Lamata P (2020) The 'Digital Twin' to Enable the Vision of Precision Cardiology. *Eur Heart J* 41(48):4556-4564

- 67. van der Lande A (2021) Developing the Digital Twin of the Acl. MSc, *Eindhoven University of Technology, The Netherlands*
- 68. Zwerver P, Janssen RPA, van der Steen MC, van Groningen B, Bulsink J, Foolen F (2021) Younger and Riskier – an in Vitro Graft Model to Investigate the Higher Risk of Acl-Graft Rupture in Younger Patients. MSc, *Eindhoven University of Technology, The Netherlands*
- 69. Dede Eren A, Singha R, Deniz Eren E, Huipin Y, Gulze-Iz S, Valster H, Monroni L, Foolen J, de Boer J (2020) Decellularized Porcine Achilles Tendon Induces Anti-Inflammatory Macrophage Phenotype in Vitro and Tendon Repair in Vivo. *Journal of Immunology and Regenerative Medicine* 8
- 70. Spierings J (2020) A Novel Concept in Acl Reconstruction Surgery: An Off-the -Shelf Decellularized and Sterilized Bone-Acl Allograft. MSc, *Eindhoven University of Technology, The Netherlands*
- 71. Kimenai JN (2019) A Microtissue Platform as Screening Method for Acl Reconstructive Surgery Outcome: Towards Personalized Rehabilitation. MSc, *Eindhoven University of Technology, The Netherlands*
- 72. Stefanoska D (2018) Mechanical Behaviour of Human Hamstring Tendons Used as Autografts in Acl Reconstruction. MSc, *Eindhoven University of Technology, The Netherlands*
- 73. Idenburg PJ, WEmonts S, Chavannes N (2020) Zorg Enablers 2020: Technologische Ontwikkelingen in De Gezondheidszorg. 4th Ed., 4th Ed. edn.,
- 74. Janssen RPA (2021) Lectoraat Value-Based Health Care. Fontys University of Applied Sciences. <u>https://fontys.nl/Over-Fontys/Fontys-Paramedische-Hogeschool/Onderzoek/Interprofessioneel-Samenwerken/Lector-dr.-Rob-Janssen.htm</u>. Accessed February 14 2021
- 75. van Vijven M, Kimenai JN, van Groningen B, van der Steen MC, Janssen RPA, Ito K, Foolen F (2021) A Patient-Specific Microtissue Platform to Compare Biological Properties in Vitro with Patient Outcome for Anterior Cruciate Ligament Reconstruction. *Orthopaedic Proceedings* 103-B(4)
- 76. de Vos FH, Meuffels DE, Janssen RPA, Liu W, Reijman M (2020-) Acl Algorithm Study: The Rotate Trial.
- 77. Eijgenraam SM (2020) The Meniscus Matters-Novel Insights into Imaging and Treatment of Meniscal Pathology. PhD, *Erasmus University Rotterdam, The Netherlands*
- 78. Rietbergen T, Maren-van de Mheen PJ, Diercks RL, Janssen RPA, van der Linden-van der Zwaag HMJ, Nelissen RGHH, Steyerberg EW, van Bodegom-Vos L, Group SS (2021) Performing a Knee Arthroscopy among Patients with Degenerative Knee Disease: One-Third Is Potentially Low Value Care. *Knee Surg Sports Traumatol Arthrosc*, June 19, 2021,
- 79. du Perron L (2021) Artroscopie Van De Knie Is Niet Altijd Zinnige Zorg. *Ned Tijdschr Geneeskd* 165:C4928
- 80. van Eijck S, Janssen DM, van der Steen MC, Delvaux E, Hendriks JGE, Janssen RPA (2021) Ehealth Applications to Make a Primary Diagnosis in Orthopedic Surgery: A Scoping Review. *Knee Surg Sports Traumatol Arthrosc* (under review)
- 81. Gaasbeek D (2021) Multidisciplinary Project on Patient-Specific Prediction Models by Modelling a Digital Twin Knee. *Eindhoven University of Technology*
- 82. Morrenhof K (2021) Translating Radiographs into Clinical Dashboard Data for Future Use in Digital Twin Modeling of the Knee. *Eindhoven University of Technology*
- 83. Sakovic J (2021) Conceptual Database Design of the Acl Patient's Data. *Eindhoven University of Technology*