ERASMUS UNIVERSITEIT ROTTERDAM

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Department of Radiology, Erasmus MC Rotterdam In close collaboration with Departments of Medical Informatics, General Practice, and Internal Medicine, Erasmus MC Rotterdam
Project Title:	Validation of cartilage and meniscus composition in early knee osteoarthritis measured with novel T2 mapping MRI against clinical and genetic determinants: the Rotterdam Study.
Abstract:	Osteoarthritis (OA), the most common degenerative joint disease, is influenced by hormonal status, metabolic health, and genetics with heritability of 40-60%. OA can be imaged with traditional morphological MRI visualizing morphological tissue alterations e.g. cartilage loss, osteophytosis, meniscal degeneration, synovitis, etc. However, since morphological changes manifest only with advanced OA, morphological MRI cannot detect early OA and subtle OA progression. Moreover, correlation of morphological MRI with OA symptoms is variable. T2 mapping is a novel quantitative MRI technique measuring collagen content in joint tissues occurring in initial OA before onset of morphological damage, which enables much earlier OA detection. T2 mapping is useful to objectively and reproducibly compare collagen content of cartilage and meniscus. There is no published application of T2 mapping MRI in a population-based study with systematic evaluation against morphological MRI and correlation with OA symptoms and genetics. In this project, validation of T2 mapping will be performed against clinical and genetic markers in the Rotterdam Study, one of the largest OA studies. Our large unselected open population-based study of females in a menopausal transitional period with a wealthy set of prospectively collected data including metabolic, hormonal and genetic markers, and bilateral knee MRI with 6 years follow-up is unparalleled. This is the only Dutch and one of few OA studies world-wide applying T2 mapping in a population imaging setting. <u>Hypothesis</u> We hypothesize that cartilage and meniscus composition measurements with novel T2 mapping MRI offer additional value over morphological MRI and aim to: 1. Validate T2 mapping MRI abnormalities against radiographic knee OA severity and investigate within-subject T2 mapping outcome

	differences in unilateral OA; 2. Evaluate associations between T2 mapping outcomes and hormonal, metabolic, and genetic markers; 3. Establish correlations of quantitative T2 mapping outcomes with OA features on morphological MRI, and the additional value T2 mapping over morphological MRI; 4. Determine the additional value of T2 mapping over morphological MRI in terms of improved correlation with OA symptoms. Work plan We will study 690 women aged 45-60 years with T2 mapping MRI at 6 years follow-up, constituting a nested cohort of the Rotterdam Study, a prospective, population-based cohort among inhabitants aged ⩾45 years of Rotterdam's Ommoord district. All MRI scans have already been acquired and are available for analysis. Knee radiography and morphological MRI of both knees are also available at baseline and follow-up. T2 mapping MRI will be analyzed with advanced in-house developed post-processing software. Knee OA related clinical data are collected with validated questionnaires. Hormonal status and metabolic health information is collected by questionnaire and endocrinological and lipid metabolism serum measurements. A genome-wide genotype database containing 550000 (and 2.5 million imputed) single nucleotide polymorphisms and 49229 copy number variations is also available for correlation. Expected outcome This project will provide validation of a novel OA imaging biomarker – T2 mapping MRI – in a large open population-based study. We anticipate that this biomarker will demonstrate additional value over morphological MRI, being more sensitive and correlating better with clinical OA symptoms. T2 mapping is expected to be a promising new OA associated imaging biomarker and target measure for clinical trials. Corroborated by our findings, T2 mapping MRI has great potential to become a feasible and widely used imaging biomarker for OA research and even patient care.
Requirements of candidate:	The candidate is expected to: - Have a background in medicine and/or image analysis (e.g. bio-engineering), or equivalent; - Have an affinity with medical imaging (radiology) and advanced quantitative magnetic resonance imaging (MRI), including the image post-processing and analysis;

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	- Be interested in the analysis of MRI outcomes with epidemiological and genetic correlates. The knowledge of genetic analysis is not required. Master degree: Yes IELTS Grade: 7.0 *(minimal 6.0 per component)* *or* TOEFL: *100 (minimal 20 per component)*
Supervisor information:	Overall supervisor: Prof. dr. G.P. Krestin, MD, PhD Department chair Department of Radiology g.p.krestin@erasmusmc.nl http://www.erasmusmc.nl/radiologie/?lang=en Primary supervisor: Dr. Edwin H.G. Oei, MD, PhD Assistant professor of musculoskeletal imaging Department of Radiology, Erasmus MC Rotterdam e.oei@erasmusmc.nl http://www.roar-nl.com/imaging <u>Recent publication list of Dr. Edwin Oei, MD, PhD</u> 1. Van Tiel J, Siebelt M, Waarsing JH, Piscaer TM, Van Straten M, Booij R, Dijkshoorn ML, Kleinrensink GJ, Verhaar JAN, Krestin GP, Weinans H, **Oei EHG.** CT arthrography of the human knee to measure cartilage quality with low radiation exposure. Osteoarthritis and Cartilage 2012 Jul;20(7):678-85. 2. Bron EE, Van Tiel J, Smit H, Poot DHJ, Niessen WJ, Krestin GP, Weinans H, **Oei EHG**, Kotek G, Klein S. Image registration improves human knee cartilage T1 mapping with delayed gadolinium-enhanced MRI of cartilage (dGEMRIC). European Radiology 2013 Jan;23(1):246-52. 3. Van Tiel J, Kotek G, Smit H, Bron E, Klein S, Krestin GP, Weinans H, **Oei EHG.** Reproducibility of 3D delayed gadolinium enhanced MRI of cartilage (dGEMRIC) of the knee at 3.0 T in patients with early stage osteoarthritis. European Radiology 2013 Feb;23(2):496-504. 4. Oei L, Rivadeneira F, Breda S, Zillikens MC, Hofman A, Uitterlinden AG, **Oei EHG.** Review of radiological scoring methods of osteoporotic vertebral fractures for clinical and research settings. Eur Radiol 2013 Feb;23(2):476-86. 5. Oei L, Zillikens MC, Dehghan A, Castano-Betancourt MC, Estrada K, Stolk, **Oei EHG**, Van Meurs JBJ, Hofman A, Beck TJ, Pols HAP, Janssen JAMJL, Witteman JC, Van Leeuwen JPTM, Uitterlinden AG, Rivadeneira F. High bone mineral density and fracture risk in type 2 diabetes as skeletal complications of inadequate glucose control: the Rotterdam Study. Diabetes Care. 2013 Jun;36(6):1619-28. 6. De Schepper EIT, Overdevest GM, Suri P, Peul WC, **Oei EHG**, Koes BW, Bierma-Zeinstra SMA, Luijsterburg PAJ. Diagnosis of lumbar spinal stenosis. An updated systematic review of the accuracy of diagnostic tests. Spine (Phila Pa 1976). 2013 Apr 15;38(8):E469-81. 7. Makurthou AA, Oei L, El Saddy S, Breda SJ, Castaño-Betancourt MC, Hofman

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9. Kerkhof HMJ, Bierma-Zeinstra SMA, Arden NK, Metrustry S, Castano-Betancourt MC, Hart DJ, Hofman A, Rivadeneira F, **Oei EHG**, Spector TD, Uitterlinden AG, Janssens ACJW, Valdes AM, Van Meurs JBJ. Prediction model for knee osteoarthritis incidence, including clinical, genetic and biochemical risk factors. Ann Rheum Dis. 2013 Aug 20. [Epub ahead of print]
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11. Breda SJ, Oei L, **Oei EHG**, Zillikens MC. Osteoporotic vertebral fractures or Scheuermann's disease? Ned Tijdschr Geneeskd. 2013;157(45):A6479
12. Van Tiel J, Reijman M, Bos PK, Hermans J, Van Buul G, Bron EE, Klein S, Verhaar JAN, Krestin GP, Bierma-Zeinstra SMA, Weinans H, Kotek G, **Oei EHG.** Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) shows no change in cartilage structural composition after viscosupplementation in patients with early-stage knee osteoarthritis. PLoS One. 2013 Nov 6;8(11):e79785.
13. Oei L, Ly F, El Saddy S, Makurthou AA, Hofman A, Van Rooij FJA, Uitterlinden AG, Zillikens MC, Rivadeneira F, **Oei EHG.** Multi-functionality of computer-aided quantitative vertebral fracture morphometry analyses. Quant Imaging Med Surg. 2013 Oct;3(5):249-55.
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	Zeinstra SMA. Malalignment: a possible target for prevention of incident knee osteoarthritis in overweight and obese women. Rheumatology (Oxford). 2014 Apr 4. 21. Van Tiel J, Kotek G, Reijman M, Bos PK, Bron EE, Klein S, Verhaar JAN, Krestin GP, Weinans H, **Oei EHG.** Delayed gadolinium-enhanced MRI of the meniscus (dGEMRIM) in patients with knee osteoarthritis: relation with meniscal degeneration on conventional MRI, reproducibility, and correlation with dGEMRIC. Eur Radiol. 2014 May 10. [Epub ahead of print] 22. Damen J, Schiphof D, Wolde ST, Cats HA, Bierma-Zeinstra SMA, **Oei EHG.** Inter-observer reliability for radiographic assessment of early osteoarthritis features: the CHECK (cohort hip and cohort knee) study. Osteoarthritis Cartilage. 2014 Jul;22(7):969-74.. 23. Van Meer BL, **Oei EHG**, Bierma-Zeinstra SMA, Van Arkel ER, Verhaar JA, Reijman M, Meuffels DE. Are magnetic resonance imaging recovery and laxity improvement possible after anterior cruciate ligament rupture in nonoperative treatment? Arthroscopy. 2014 Jun 17. [Epub ahead of print] 24. Runhaar J, Schiphof D, Reijman M, Bierma-Zeinstra SMA, **Oei EHG**. How to define progression of osteoarthritis using semi-quantitative MRI Osteoarthritis Knee Score (MOAKS). Osteoarthritis and Cartilage (In press) 25. Van Ochten JM, Mos M, Van Putte-Katier N, **Oei EHG**, Bindels PJ, Bierma-Zeinstra SMA, Van Middelkoop M. Structural abnormalities after an ankle sprain are not associated with persistent complaints. Br J Gen Pract (In press) 26. Roels P, Campoli G, Agricola R, **Oei EHG**, Weinans H, Zadpoor AA. Mechanical factors explain development of cam-type deformity. Osteoarthritis Cartilage (Accepted)