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Progress Report

	Description
1. Date	December 27, 2011
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3. Project leader(s)	Carla H van Gils, PhD; Petra HM Peeters, MD PhD; Willem PThM Mali, MD PhD
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5. Title Project	Early detection of breast cancer in women with dense breasts
6. How many patients are involved in this project / are there others involved in the implementation of the project	For this project, around 4,700 women with extremely dense breast tissue and a 'negative' screening mammogram will be invited for additional MRI. Around 28,000 women with extremely dense breast tissue and a 'negative' screening mammogram as well form the control group and participate in the regular breast cancer screening. For this project 6 hospitals, specialized in breast MRI, are involved as well as all five regional screening organisations in the Netherlands.
7. Summary of progress of project	Start date project: January 1st, 2011 Research question: What is the (cost) effectiveness of biannual screening with mammography + MRI for women with extremely high dense breast tissue? Research design: Randomized controlled trial – Screening participants with extremely high dense breast tissue will be randomized to: 'biannual mammography + MRI' (n=7,237) or biannual mammography (n=28,948). Primary outcomes are numbers of breast cancer detection and interval tumour rates in each group. The study has been set up and collaborations have been established with all organisations that are involved in the nationwide population-based breast cancer screening in the Netherlands. We prepared the application for a license to carry out this research, conform the Population Screening Act (Wet Bevolkingsonderzoek, WBO). The Health Council recommended the study and the Minister of Health approved the study in November 2011. Over the last year, all preparations have been taken, including development of all selection- and MRI protocols, extensive lifestyle, medical and quality of life questionnaires and patient information. Registration of participants and all questionnaires are fully digital. Software for measuring breast density full-automatically is now being tested in the screening units. We have further validated this software. The first participants from the region "Midden-West" have been enrolled in the study.

8. Results (detailed description)	**Results – detailed description:** December 2010, we submitted the application for the license from the Ministry of Health that is required conform the Population Screening Act (Wet Bevolkingsonderzoek, WBO). Meanwhile, we prepared all work for this large multi-center trial. *- Authorization Minister of Health* The Health Council of the Netherlands recommended the Minister of Health to authorize the DENSE study. An authorization by the Minister of Health was approved at November 11th 2011. *- Data collection* All preparations have been taken in the past year, including development of protocols, extensive lifestyle, medical and quality of life questionnaires and patient information. Registration of participants and all questionnaires are fully digital. For this, a special online data management system has been developed. Software for automatically measuring breast density has been further validated. The software is now being tested in the screening units. *- Collaborations* In the past year, much time and effort has been spent on setting up collaborations with all organizations that play a role in the current breast cancer screening program. These are the 5 breast cancer screening organizations (Midden-West, Zuid-West, Noord, Oost en Zuid), the National Expert and Training Center for Breast Cancer Screening (LRCB), the Center for Screening of the National Institute for Public Health and the Environment (CvB-RIVM), the 6 MRI specialized centers For the quality of life analysis and cost-effectiveness analysis we collaborate with researchers from Erasmus UMC. They are specialized in working with breast cancer microsimulation models (MISCAN). The Breast Cancer Patient Organization (Borstkanker vereniging) supports our trial too. *- Start of the study* Immediately after we obtained the license (November 2011), we started in the region Midden-West with the selection and randomization of women who fulfilled the inclusion criteria. They have been invited in writing and the first participants have been enrolled. In 2012 the study will be unrolled in the other screening regions.
9. Short description in Dutch	**Vroegdiagnostiek van borstkanker bij vrouwen met mammografisch 'dense' borstweefsel: DENSE studie** Vrouwen met een zeer hoge mammografische densiteit van het borstweefsel (veel klier- en bindweefsel in de borst, weinig vetweefsel) hebben een 3-6 keer zo hoge kans op borstkanker als vrouwen met een lage densiteit. Mammografische densiteit is dus één van de belangrijkste risicofactoren voor borstkanker. Bovendien zijn eventueel aanwezige borsttumoren veel moeilijker te ontdekken bij deze vrouwen, doordat het dense borstweefsel de aanwezigheid van borstkanker op een röntgenfoto kan verbergen. Deze vrouwen zijn daarom mogelijk gebaat bij borstonderzoek met gevoeligere apparatuur, zoals MRI. Het doel van de DENSE studie is om bij vrouwen tussen de 50 en 75 jaar met dense borstweefsel die deelnemen aan het 2-jaarlijkse bevolkingsonderzoek te onderzoeken, of tumoren eerder ontdekt kunnen worden met een combinatie van MRI en mammografie dan met mammografie alleen. Ook wordt onderzocht of bij het MRI onderzoek niet teveel vrouwen onnodig worden verwezen voor nader onderzoek en of de baten opwegen tegen de kosten.

	De DENSE studie richt zich op vrouwen die meedoen met het reguliere bevolkingsonderzoek borstkanker. Vrouwen komen in aanmerking voor de studie wanneer ze dense borstweefsel hebben én geen verdachte afwijking op het mammogram is te zien. Ongeveer 5000 vrouwen zullen willekeurig, op basis van loting, geselecteerd en uitgenodigd worden voor aanvullend MRI onderzoek. De vrouwen zullen zes jaar worden gevolgd en krijgen dus in totaal drie MRI-onderzoeken (na elke reguliere screeningsronde). De resultaten in deze groep worden vergeleken met die van het reguliere bevolkingsonderzoek borstkanker.
10. Allocated amount of funding	100,000 euro
11. Grants obtained from other organizations	Besides A Sisters Hope, also KWF Kankerbestrijding, ZonMW Preventie, Bayer Pharma AG, and UMC Utrecht support the first screening round of the DENSE study. Finance for the upcoming screening rounds will be requested next year.
12. Remarks	We thank A Sisters Hope for their financial support for this research. The subject of this study is a hot topic in the (Dutch) society. Questions have been raised in the parliament about screening options for women with dense breast tissue and the Minister of Health expressed her support to our study in several ways. A Sister's Hope support is very important to make this study a success.