A predictive profile for ipsilateral invasive breast cancer in patients with in-situ breast cancer

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Aim

This proposal aims to test whether a combination of clinical, immunohistochemical and genetic profiling, the latter established by the novel powerful method of low coverage sequencing and targeted sequencing (i.e. next generation sequencing techniques), can be used to distinguish DCIS lesions associated with a very low risk of a subsequent invasive breast cancer in the same breast (iiBC). Our proposal will generate a novel insight in the association of DCIS with the subsequent development of invasive breast cancer.

Current status

1. At the moment we are collecting paraffin embedded tissue blocks from patients who have been treated with BCS alone. In our project, women who have developed a subsequent iiBC are considered cases. For each case, we have selected 4 age-matched controls, i.e. women who did not develop any other subsequent breast event after the first DCIS diagnosis within the same follow-up time, within the same treatment group. We have identified these patients by linking data from the Netherlands Cancer Registry with data from PALGA, the Dutch nationwide network for histology and pathology and tracing back remaining archived pathology specimen. So far, we have send out requests to 58 pathology labs and obtained the requested paraffin embedded tissue blocks and HE-slides from 64% of the pathology laboratories (see Figure 1). Currently 7 pathology laboratories did not want to participate in the study, we are talking about participation with 8 other labs. In two months time we expect to have material from 1100 DCIS and 250 invasive breast cancers. For a good assessment of the lesions by our breast pathologist we are now currently preparing new HE-slides, as most of the slides we have received are of insufficient quality for pathology review.
2. We are evaluating the best method to retrieve sufficient DCIS tissue from the formalin-fixed, paraffin embedded tissue blocks by state-of-the art micro-dissection techniques to enable efficient isolation of sufficient quantities of DNA and RNA for further molecular analyses. This is done by a recently started molecular biology PhD student (Lindy Visser, appointed May 2014). She will set up a proper analysis pipeline for the DCIS lesions to obtain DNA of sufficient quality and quantity for molecular analysis.
3. We decided to use low-coverage Next Generation Sequencing (shallow-seq), instead of array Comparative Genomic Hybridization, mentioned in the original grant application, as a more up-to-date technique providing more 'high resolution' and more informative data without compromising the available budget. This method is up and running in our institute.

Planned time Schedule

During the first 6-9 months we planned to retrieve tissue blocks from Dutch Pathology laboratories. During months 6-12 we will perform targeted sequencing. In year two we will perform statistical analysis and report our findings.

Future perspective

We are on schedule to due review the cases and perform the molecular analysis. This implies that we hope to finish this part of our research on time.

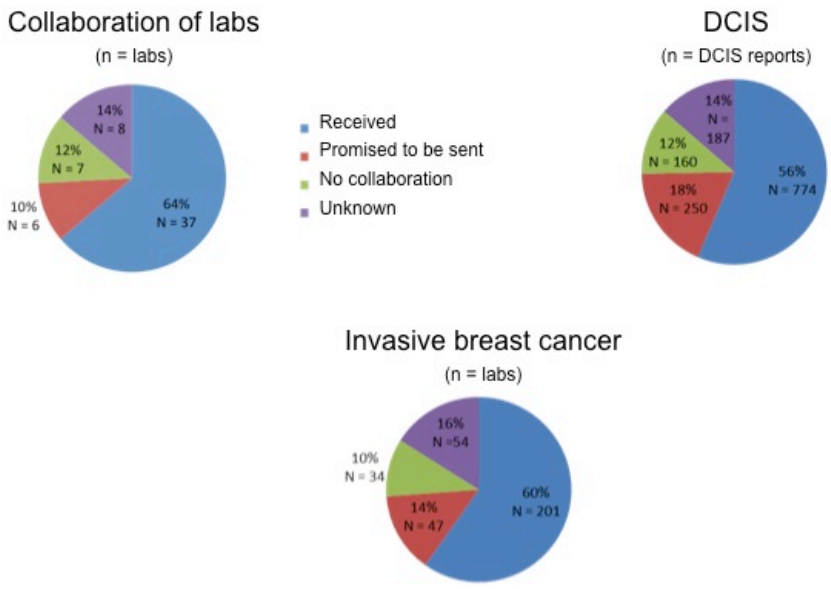

Figure 1: Overview of number of collaborating labs