Market Research within the Pharmaceutical Industry

A Case study of SPAGO Imaging AB

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Preface

This master thesis was performed as a last step in the completion of my education towards a Master of Science degree at Lund Institute of Technology. The thesis was made at the division of Production Management in the department of Industrial Management and Logistics.

I would like to thank all the people involved in the process of this project. I would especially like to thank my supervisor at Lund Institute of Technology, Ingela Elofsson, for her guidance and support throughout the project and my supervisor at SPAGO Imaging AB, Oskar Axelsson, for always taking time and effort to help me with my questions and thoughts.

Last but not least, I would like to thank my family for their support and encouragement during my whole education time here at Lund University.

Lund, December 2009

Angelica Rönnholm

Abstract

Title: Market Research within the Pharmaceutical Industry – A Case study of SPAGO Imaging AB

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Problem definition: SPAGO Imaging AB is developing a new contrast agent for Magnetic Resonance Imaging (MRI). In approximately 5 years, the product will be launched on the market. The company is therefore about to look for investors to fund the development and growth. To gain investors interest, a clearly defined market for this sort of contrast agent is required.

Purpose: The purpose of this thesis is to analyze the market of SPAGO Imaging AB´s contrast agent in the field of breast cancer.

Methodology: The approach of the theses was a survey study because the interest was to gather basic knowledge from many fields. The study is based primarily on secondary data, gathered through books, scientific papers and various websites. The secondary data was complemented with primary data, collected through personal interview and internet surveys with three radiologists. Most of the collected data is qualitative in nature.

Conclusions: Breast cancer is the most frequency diagnosed malignancy in women. The most widely used screening test to detect breast cancer is mammography, but mammography involves ionizing radiation that can produce adverse health effects and the sensitivity of the test is limited (79%).

Magnetic Resonance Imaging is a valuable complementary modality to conventional screening methods. The strength

of the MRI technology is the high sensitivity (92.5%). MRI also uses radio-frequency waves, which is non-ionizing energy and considered safe. Nevertheless, breast MRI has played a limited role in cancer detection. It is probably due to a combination of a low specificity (72.4%) and the significantly higher cost.

The new contrast agent, developed by SPAGO Imaging AB, will most likely give a higher specificity and a higher sensitivity. The product will however not change the fact that the MRI is not appropriate for general screening. The reason for that is the high cost together with the long waiting time after the administration of the contrast agent.

The screening has, however, become more individual-based and women with increased risk for developing breast cancer need a more sensitive screening tool. The contrast agent of SPAGO Imaging AB is therefore suitable for screening women with high risk of developing breast cancer.

Diagnostic tests are used to classifying the tumors and to gather more information about the cancer. For the purpose of determining the size and location of the tumors the most common methods are mammography and sonography.

However, the high soft tissue contrast and three-dimensional format of MRI allows anatomic structures of the breast to be viewed in greater detail. Why the MRI technique isn't used to a higher extent for diagnostic purposes probably depends on a combination of a lack of availability and the risk of overestimating the extent of disease. SPAGO Imaging AB´s contrast agent will most likely give a better contrast so the diagnostic area is also a potential segment.

Keywords: Market Research, Contrast Agent, Magnetic Resonance Imaging, Product Development

Abbreviations

AAGR — Average Annual Growth Rate

ACR — American College of Radiology

ACS — American Cancer Society

BMC — Biomedical Center

BRCA1 — Breast Cancer susceptibility gene 1

BRCA2 — Breast Cancer susceptibility gene 2

BSE —Breast Self-Examination

BPE —Breast Physical Examination

CBEV —Clinical Breast Examination

CISH —Chromogenic In Situ Hybridization

CMIV — Center for Medical Image Science and Visualization

CNB — Coarse-Needle Biopsy

CT— Computerized Tomography

DCIS — Ductal Carcinoma In Situ

DL — Ductal Lavage

EC — European Commission

ELIN — Electronic Library Information Navigator

EU—European Union

FDA — U.S. Food and Drug Administration

FNA — Fine-Needle Aspiration

GBCA — Gadolinium-Based Contrast Agents

Gd — Gadolinium

LTH — Lund Institute of Technology

MRI — Magnetic Resonance Imaging

NAF — Nipple Aspirate Fluid

NC — Not Calculated

NCI — National Cancer Institute

NFD — Nephrogenic Fibrosing Dermopathy

NSF — Nephrogenic Systemic Fibrosis

PET — Positron Emission Tomography

PLoS — Public Library of Science

R&D — Research and Development

SPAGO — Safe Paramagnetic Gadolinium Oxide nanoparticles

SWOT — Strengths Weaknesses Opportunities Threats

WHO — World Health Organization

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1. Introduction

In chapter one the reader is first introduced to the company SPAGO Imaging AB, followed by a background and problem discussion. Second, the purpose of the master thesis is being established as well as the targeted group. Finally, a brief overview is given of the structure of this report.

1.1 Company Presentation

"*Market Research within the Pharmaceutical Industry - A Case study of SPAGO Imaging AB*" is the title of this master thesis which was written in cooperation with the company SPAGO Imaging AB. SPAGO Imaging AB is a small R&D company located in Lund, Sweden. The company develops a nanoparticle-based contrast agent for Magnetic Resonance Imaging (MRI) with applications in tumor diagnostics and the cardio-vascular field.[1]

1.1.1 Vision

The long-term vision of SPAGO Imaging AB is the following:

"Be a world leading translational R&D company for in-vivo diagnostics supplying partners with strong projects for commercialization."[2]

1.1.2 History

SPAGO Imaging AB is a relatively new company, founded in the year of 2007 in Linköping, Sweden. The business idea is based on research about nanoparticle-based contrast agents as part of a project called Spago Enhanced MRI (formerly known as MRI Boost).[3]

Dr. Kajsa Uvdal, a physicist at Linköping University, managed to create nanoparticles of Gadolinium oxide. To get a medical application of the nanoparticles, Kajsa Uvdal turned to Dr. Maria Engström, a researcher at the Center for Medical Image Science and Visualization (CMIV) at the University Hospital in Linköping. Maria Engström was at the time working with a technique

[1] Homepage of SPAGO Imaging AB, *Home* [Online]
[2] Axelsson, O., personal communication, August 17, 2009
[3] Axelsson, O., personal communication, August 17, 2009

called *Magnetic Resonance Imaging,* in order to take pictures of the body's interior.[4]

Magnetic Resonance Imaging uses a powerful magnetic field, radio frequency pulses and a computer to produce three-dimensional images of the body's interior.[5] For better contrast, patients get injected with a *contrast agent*. These agents improve the contrast of MRI images by increasing the brightness in various parts of the body where the agent resides. The most common contrast media used today is made up of individual atoms of gadolinium.[6]

The contact between Maria Engström and Kajsa Uvdal led to the idea that the newly developed nanoparticles could be used as a contrast agent to enhance signals in the MRI scanner. The promising results from the studies prompted the inventors to submit two patents, which later were licensed to Accelerator Nordic AB (then Accelerator i Linköping AB).[7]

After some small scale efforts to bring the project forward in an academic setting, a decision was made to form a company and employ qualified staff to bring the project forward to a state that could either attract licensees or investors. In March 2007 Rodrigo Petoral, a former PhD student of Uvdal, was hired and a few months later Oskar Axelsson, with a background in MR contrast- and nanoparticle research from GE-healthcare, joined.

The company is, since January 2008, located in the Ideon Bioincubator at BMC, Lund, and has in the current situation three fulltime and one halftime employees.[8]

1.1.3 Organization

SPAGO Imaging AB is a subsidiary of Accelerator Nordic AB, located in Stockholm. Accelerator Nordic AB owns a number of companies within the area of Life Sciences. Among the companies are, in addition to SPAGO Imaging AB, PledPharma AB, which develops pharmaceutical applications, Synthetic MR AB, which develops software for time-saving synthetic MRI, OptoQ AB which markets

[4] Engelmark Cederborg, S., 2006, *Partiklar med potential* [Online]
[5] Homepage of RadiologyInfo, *MRI of the Body (Chest, Abdomen, Pelvis)* [Online]
[6] Axelsson, O., personal communication, September 8, 2009
[7] Axelsson, O., personal communication, September 8, 2009
[8] Axelsson, O., personal communication, September 8, 2009

and sells systems and technology platforms for patient monitoring and Optovent AB which develops and commercializes research-based innovations.[9]

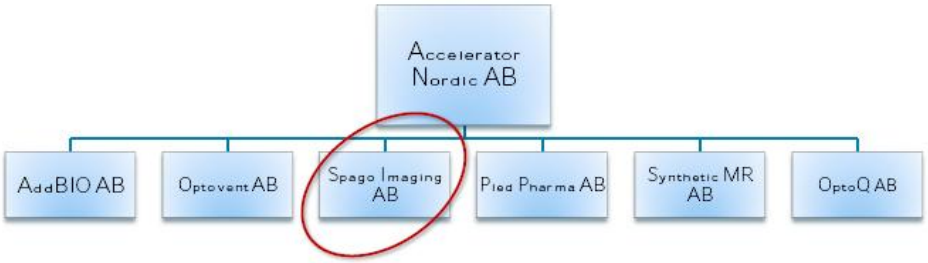

Figure 1.1 – The organization of Accelerator Nordic AB.[10]

1.2 Background and Problem Discussion

SPAGO Imaging AB is currently about to enter a formal preclinical phase where the stability of the particles has been secured and verified. There is an estimated five years until the contrast agent will be launched on the market.[11] At this important stage of development the company is facing a major business challenge: to move from a research company to a company that have a commercial product out on the market. Therefore, the company is about to look for investors to fund the development and growth. To get investors interested it requires a clearly defined market for this sort of contrast agent.

The product of SPAGO Imaging AB is an MRI contrast agent, meaning that the contrast agent can only be used together with the Magnetic Resonance Imaging technology. MRI is a relatively new technology which has completely revolutionized the field of medical imaging. The technique is used for detecting abnormalities or lesions in most parts of the body and is administered to patients suffering from the following:[12]

- Cancer
- Degenerative diseases
- Inflammation or Infection
- Strokes
- Musculoskeletal disorders

[9] Homepage of Accelerator Nordic AB, *Om Accelerator* [Online]
[10] Axelsson, O. (oskar.axelsson@spagoimaging.se), 3 November 2009 [e-mail]
[11] Axelsson, O., personal communication, September 8, 2009
[12] Homepage of University of Windsor, *Applications of MRI* [Online]

The selected area for this study was cancer because it is a widespread disease, with more than eleven million people diagnosed with it every year. The area has also several applications for the MRI technology and there are indications that progress in the MRI field may give medical benefits.

Cancer is, however, not a single disease but a group of diseases of which there are over a hundred types.[13] It has therefore, due to time constraints, been necessary to limit the scope of the study to only one form of cancer, namely breast cancer.

Breast cancer is the second most common cancer worldwide, with over one million new cases each year.[14] Death rates from breast cancer have been steadily decreasing due to a combination of early detection and improved treatment. Nevertheless, half of all patients diagnosed with breast cancer will die from the disease.[15] The greatest potential for a reduction in mortality is earlier detection and more accurate diagnoses, so new, better methods are urgently needed. Breast cancer is therefore a very interesting market field for SPAGO's contrast agent.

1.3 Purpose of the Thesis

The main purpose of this thesis is to analyze the market of SPAGO Imaging AB´s product in the field of breast cancer. This requires separate analysis of the MRI market and SPAGO´s contrast agent. The study will therefore include both an analysis of the current methods to identify breast cancer, as well as an analysis of the properties of SPAGO´s product.

1.4 Target Group

This master thesis is written for two separate targeted groups; the management of SPAGO Imaging AB and senior students with a business or engineering background.

[13] Zebrowski, M., 2007, p. 19
[14] Center, M., Garcia, M., Hao, Y., Jemal, A., Siegel, R., Thun, M. & Ward, E., 2007, p. 3
[15] Bruening, W., Kostinsky, H., Launders, J., Pinkney, N., Schoelles, K. & Turkelson, C., 2006, p. 5

1.5 Structure of the Thesis

This thesis is structured in seven main chapters. Following is an overview of what each chapter in short offers:

Chapter 1 – Introduction

In chapter one the reader is first introduced to the company SPAGO Imaging AB, followed by a background and problem discussion. Second, the purpose of the master thesis is being established as well as the targeted group. Finally, a brief overview is given of the structure of this report.

Chapter 2 – Methodology

Chapter two serves as guidance for the reader in order to explain how the data have been managed and which methodological approaches have been utilized to penetrate the issues covered in this thesis. Different study approaches, as well as different data collection methods, are discussed. This is followed by a description of the collection process of both primary and secondary data and the section ends with a discussion of validity, reliability and how criticism of the sources have been handled.

Chapter 3 – Theory

In chapter three the theory used for the master thesis is presented. The theory includes different definitions relevant to the thesis, as well as tools and methods used in the analysis.

Chapter 4 – Empirics: Cancer and Methods for Cancer Detection

Chapter four contains information about cancer, breast cancer, as well as current techniques to detect breast cancer.

Chapter 5 – Analysis of the MRI technology

Chapter five contains an analysis of the MRI technology. The advantages and disadvantages, as well as possible areas for improvement, of the technology are discussed.

Chapter 6 – Empirics and Analysis of SPAGO´s contrast agent

Chapter six contains a description of SPAGO´s contrast agent and a brief overview of the market of MRI and the existing contrast agents. The chapter also includes a SWOT analysis of SPAGO´s product.

Chapter 7 – Summary and Reflections

Chapter seven summarizes the impressions from the empirics and the analysis. The most important findings are brought together and form the basis of the presented recommendations.

2. Methodology

Chapter two serves as guidance for the reader in order to explain how the data have been managed and which methodological approaches have been utilized to penetrate the issues covered in this thesis. Different study approaches, as well as different data collection methods, are discussed. This is followed by a description of the collection process of both primary and secondary data and the section ends with a discussion of validity, reliability and how criticism of the sources have been handled.

2.1 Methodological Approach

The methodology is the overall approach used throughout the study; how to go from the initial formulation of the objectives to the final results of the analysis.[16] What methodology should be chosen depends on the purpose of the study and the amount of available knowledge in the specific area.[17]

The purpose of an investigation may be of four types: *descriptive, explorative, explaining* or *predictive.*

Descriptive – A descriptive approach is used when basic knowledge already exists. The aim is to strengthen the relationship without explaining the context in the field.[18] The focus is to describe, not to understand or interpret something.[19]

Explorative – An exploratory approach is used when there is little available knowledge in the field. The aim is to obtain as much knowledge and understanding as possible about the specific area.[20]

Explaining – An explaining approach investigates causality within an area, how various factors are interrelated and what the outcome of this is.[21]

[16] Höst, M., Regnell, B., & Runeson, P., 2006, p. 29
[17] Höst, M., Regnell, B., & Runeson, P., 2006, p. 29
[18] Lekvall, P. & Wahlbin, C., 2001, p. 197
[19] Andersen, I., 1998, p. 18
[20] Davidson, B. & Patel, R., 2003, p. 12
[21] Lekvall, P. & Wahlbin, C., 2001, p. 197

Predictive **–** A predictive approach is used for studies that provide forecasts of what would probably happen if certain specified conditions exist.[22]

The type of purpose which, according to the above definitions, is best suited to this study is the explorative approach. The purpose of an exploratory survey is to gather as much knowledge as possible about a specific problem area and that conform with the intention of this thesis.[23]

In a scientific work, there are two different strategies for producing knowledge; *deduction* or *induction.* If the study is based on empirical data and the conclusions are drawn after the data is collected and analyzed, the study is *inductive*.[24] Induction is sometimes also referred to as "the road of discovery" for the reason that the purpose is to form theories using the actual knowledge.[25]

If the study is based on a theory, which is then verified or rejected by the collected data, the orientation is said to be deductive.[26] In a deductive approach the conclusions are drawn from the existing theory and therefore called "the road of proof".[27]

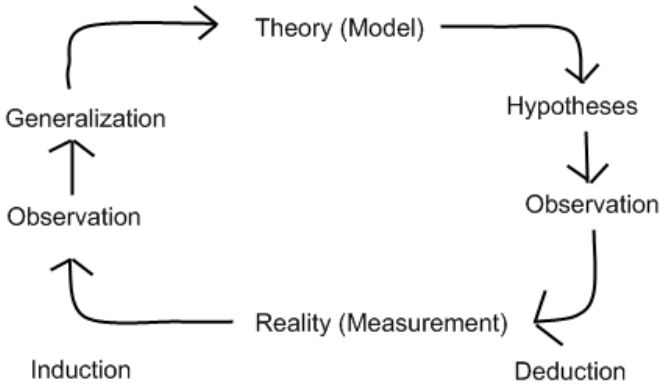

Figure 2.1 – Induction and deduction.[28]

[22] Lekvall, P. & Wahlbin, C., 2001, pp. 197-198
[23] Davidson, B. & Patel, R., 2003, p. 12
[24] Johannessen, A. & Tufte, P., 2003, p. 35
[25] Andersen, I., 1998, p. 29
[26] Johannessen, A. & Tufte, P., 2003, p. 35
[27] Andersen, I., 1998, p. 29
[28] Perolle, J., 1998 (redrawn) [e-book]

The starting point of this essay was the collected data, presented in Chapter 3, and then, from the collected data, creating a picture of the MRI market and the market for SPAGO's contrast agent. The thesis can therefore said to have an inductive approach.

The main criticism of an inductive study is that it can be difficult to draw general conclusions, since the outcome depends on the limited amount of collected data.[29] However, the purpose of this thesis is only to analyze the market of SPAGO's contrast agent and not to draw general conclusions about all actors in the MRI contrast agent industry.

2.2 Study Approach

The approach of the study has to do with its basic technical design; how we technically should proceed to draw the desired conclusions.[30] There are three main approaches to choose from:

Case study **-** In a case study just one individual or a small number of cases are analyzed. The interest is directed towards detailed and often in-depth descriptions. There is no concern in comparing the survey items with each other or to make any generalizations about an underlying population.[31]

Survey **-** Surveys are research strategies where a large number of cases are analyzed in width. A survey research is often characterized by the interest to analyze and draw conclusions about an underlying target population, to which the study units is assumed to represent. The reality is observed as it is, whiteout trying to affect it.[32]

Experimental study **-** An experimental study is also a research strategy where a large number of cases are analyzed in width, but unlike the survey approach a researcher in an experimental study actively manipulate the reality so the investigated factors become clearly highlighted.[33]

[29] Wallén, G., 1996, p. 89
[30] Lekvall, P. & Wahlbin, C., 2001, p. 209
[31] Lekvall, P. & Wahlbin, C., 2001, pp. 215-216
[32] Lekvall, P. & Wahlbin, C., 2001, pp. 216-217
[33] Lekvall, P. & Wahlbin, C., 2001, p. 210

The chosen research strategy for this thesis was the survey approach because of the purpose; to analyze and describe the market of MRI and contrast agents. To conduct that, a broad coverage was necessary.

2.3 Data Collection

2.3.1 Quantitative and Qualitative Data

The research can be based on two different kinds of data: *quantitative* or *qualitative*. Quantitative data are expressed in numerical form and often analyzed using some form of mathematical-statistical methods of calculation.[34] Qualitative data are instead information gathered from qualitative interviews or interpretive analysis. That is data that cannot meaningfully be quantified, i.e. expressed in numerical form.[35]

A qualitative approach is used to give the researcher a deeper understanding of the problem area or to gain novel understanding in a specific field. Since the purpose of this thesis is to analyze the market of MRI contrast agents, a qualitative research is adequate and therefore also chosen.

2.3.2 Primary and Secondary Data

The collected data can be divided in two groups, *primary* or *secondary* data. Secondary data is information that is already collected and compiled for another purpose. Primary data is information that the researcher collects himself from the original source.[36]

It is usually much cheaper and less time consuming to collect secondary data compared to gathering own primary data. Secondary data can also be helpful in the design of the subsequent primary research and can provide a baseline with which the collected primary data results can be compared to. Therefore, it is always wise to begin any research activity with a review of the secondary data.[37] A study based solely on secondary data is called a *desk study*.[38]

In the case of primary data, there are four common methods for collecting it: by *written questionnaires*, *face-to-face interviews*, *telephone interviews* or *Internet surveys*.

[34] Lekvall, P. & Wahlbin, C., 2001, p. 210
[35] Lekvall, P. & Wahlbin, C., 2001, p. 210
[36] Lekvall, P. & Wahlbin, C., 2001, p. 80
[37] Lekvall, P. & Wahlbin, C., 2001, p. 212
[38] Andberg, L. & Eliasson, B., 2005, p. 32

Written questionnaires – In a written questionnaire the questions are being asked and answered in writing form on a paper that is distributed and returned between the investigator and the respondent, without the intermediary of an interviewer. The big advantage of the written questionnaires is the low cost per unit. The method is therefore suitable for studies with large samples. If the questionnaires are sent by post it is often become time-consuming. There is also a risk of large losses and the control over the interview situation is weak, i.e. cannot control the order in which questions are answered in or who is actually answering the questions.[39]

Face-to-face interviews – In face-to-face interviews are the questions posed and answered verbally in a personal meeting between the interviewer and the respondent. The big advantage of the personal interview is the possibilities to make different types of questions.[40] Another major advantage of face-to-face interviews is that response rates are generally very high.[41] The major drawbacks are that they are more expensive than the other methods and that it practically can be difficult to implement.[42] The presence of an interviewer can also cause bias, i.e. socially desirable answers, and lead to misleading information.[43]

Telephone interviews – In a telephone interview are the questions posed by an interviewer and answered verbally during a telephone conversation with the respondent.[44] The properties of the telephone interviews are something between the face-to-face interview and the written questionnaires. They generally have a higher response rate than the written questionnaires but lower that the face-to-face interviews. The cost is usually less than face-to-face but higher than for the written questionnaires.[45]

Internet surveys - The questions are posed in written form on the internet, by e-mail or direct on a homepage. There is no interviewer as a link between the investigator and the respondent. The advantages are the low cost per unit and the rapidity of the method. It is also possible to have a more pedagogical layout in the

[39] Lekvall, P. & Wahlbin, C., 2001, p. 262
[40] Lekvall, P. & Wahlbin, C., 2001, p. 265
[41] Jobber, D., 2007, p. 250
[42] Jobber, D., 2007, p. 251
[43] Jobber, D., 2007, p. 251
[44] Lekvall, P. & Wahlbin, C., 2001, p. 266
[45] Jobber, D., 2007, p. 251

form of illustrations, animations and sounds. The disadvantage is a risk of large losses and a weak control over the interview situation.[46]

In order to gain novel understanding about the MRI market, a thorough desk study was conducted. Information from books, research articles and various websites was gathered. Research articles were found via Lund University Library database ELIN (Electronic Library Information Navigator). Extensive searches in various databases like the WorldWebScience, Public Library of Science (PLoS) and the PubMed database was also conducted. Lovisa, a literature catalog provided by the Lund University Library, was also used to find relevant literature.

The secondary data was also complemented with primary data. The primary data was collected by a face-to-face interview with one radiologist and internet surveys (via e-mail) with two radiologists. The face-to-face interview was chosen because of the ability for dynamics during the questioning and for the reason that the interview could be done fairly extensive. Since the other two radiologists could not attend a personal interview, internet surveys (via e-mail) were chosen.

The personal interview was of a less structured character using mostly open-ended questions, so that the respondent freely could describe the MRI market in order to receive as much information as possible. The questionnaire used for the internet surveys is presented in Appendix A.

2.3.3 Sampling Techniques

There are two different groups of sampling techniques, *probability sampling* and *non-probability sampling*. The difference between them is that probability sampling involves random selection and non-probability sampling does not. The probability of getting any particular sample can therefore only be quantitatively calculated when using a probability sampling technique.[47]

Probability sampling is mostly used within quantitative studies. Researchers who conduct qualitative studies find it difficult to adhere to the principles and procedures of probability sampling for selecting people or events. It is therefore common to use non-probability sampling techniques when conducting a qualitative research.[48]

[46] Lekvall, P. & Wahlbin, C., 2001, pp. 267-268
[47] Lekvall, P. & Wahlbin, C., 2001, p. 238
[48] Denscombe, M., 2007, pp. 29-30

The respondents of this study were chosen in collaboration with my supervisor at SPAGO Imaging AB, Oskar Axelsson and with the help of the first respondent Christer Lundahl. Because no random selection took place, the sampling method can be classified as a non-probability sampling technique.

2.4 Criticism

Two concepts are used to measure the credibility of a study; *validity* and *reliability*.[49] The aim should be to achieve as high validity and reliability as possible. However, the credibility is always balanced against the resources required for the design of the study.[50]

2.4.1 Reliability

The term reliability can be said to express the method's ability to resist influence from various coincidences.[51] With good reliability means that similar results could be obtained if the experiment was repeated.[52]

The reliability of a study can be increased through the use of control questions in surveys and interview and through the use of multiple perspectives or several types of data, i.e. *triangulation*.[53]

In this study, the striving has been to combine different types of data. Information from scientific reports, books, market statistics and personal interviews has therefore been combined in order to increase the reliability.

2.4.2 Validity

The definition of validity is the instrument's ability to measure what was intended to measure. Validity can be divided into two aspects: *internal validity* and *external validity*. Internal validity refers to the conformance between the concept and its *operationalization*. With operationalization mean how to transfer the theoretical ideas in the form of concepts and models to empirical observations. External validity has to do with the correlation between the measured value that is obtained, when using an operational definition, and the reality.[54]

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[49] Björklund, M. & Paulsson, U., 2003, p. 60
[50] Björklund, M. & Paulsson, U., 2003, p. 59
[51] Lekvall, P. & Wahlbin, C., 2001, p. 304
[52] Lekvall, P. & Wahlbin, C., 2001, p. 306
[53] Björklund, M. & Paulsson, U., 2003, p. 60
[54] Eriksson, L. & Wiedersheim-Paul, F., 2006, pp. 60-61

When using questionnaires or interviews, validity can be increased through the formulation of clear, non-biased questions.[55] The use of triangulation can also increase the validity.[56] Another thing that can increase the validity is *respondent validation*: the researcher can present the collected data in aggregate form for the persons who have been interviewed. That is a way to ensure that the participants are correctly understood.[57]

The striving has been to formulate clear, non-biased questions for the purpose to get a high validity. The respondents had also access to the report to examine if the interpretation of their contribution was correct, i.e. respondent validation.

[55] Björklund, M. & Paulsson, U., 2003, p. 60
[56] Björklund, M. & Paulsson, U., 2003, p. 60
[57] Robson, C., 2002, p. 42

3. Theory

In chapter three the theory used for the master thesis is presented. The theory includes different definitions relevant to the thesis, as well as tools and methods used in the analysis.

3.1 Definitions

The purpose of this thesis is to analyze the market of SPAGO Imaging AB´s product, but before the concept of a market research is discussed it is important to clarify the word *market*. Originally, the term *market* stood for a place where buyers and sellers gathered to exchange their goods, such as a village square.[58] Today, the term often refer to a collection of buyers in a particular product class.[59] The definition of a market is:

"*A market is the set of actual and potential buyers of a product. These buyers share a particular need or want that can be satisfied through exchanges and relationships*."[60]

There are geographic markets which relate to customers within a specific geographic area, such as the Swedish market. The market can also be defined as the application area for a particular product.[61]

In literature there are two different explanations for how a market is created. According to Armstrong & Kotler (2006) customers already exist; they do not need to be created. The company's mission is therefore to try to get, as many as possible of those, to buy the product.[62] This is sometimes called a *top-down* process because the customer is selected by the company.[63] According to other authors, such as Sarasvathy, the market is created by the company.[64] This means

[58] Hague, P., 2002, p. 4
[59] Armstrong, G., Kotler, P., Saunders, J. & Wong, V., 2005, p. 11
[60] Armstrong, G., Kotler, P., Saunders, J. & Wong, V., 2005, p. 11
[61] Olsson, J. & Skärvad, P.-H., 2003, p. 241
[62] Armstrong, G. & Kotler, P., 2006, p. 40
[63] Stokes, D., 2000, p. 51
[64] Sarasvathy, S., 2001, p. 244

that some customer group will be selected by the company and other groups will be ignored; it becomes a so-called *bottom-up* process.[65]

Regardless of the view to how the market is created, the company must try to understand the customers and their needs. This is done by analyzing the market, i.e. by conduct a *market research*.[66]

A market research is any organized effort to gather information about markets or customers. It is an important component of business strategy.[67] The role of market research is simply to strive to coordinate and concentrate a firm's total resources to those parts of the market where the greatest likelihood of success are.[68]

As mentioned earlier, the market consists of both actual and potential buyers. These buyers differ in one or more ways. They can have different needs, resources, locations and buying attitudes.[69] Companies cannot satisfy all these different consumers, there a too many kinds of them with too many kinds of needs. Consequently, companies use *market segmentation* to divide the total market.[70] Market segmentation is defined as follow:

"(…) *the identification of individuals or organizations with similar characteristics that have significant implications for the determination of marketing strategy*".[71]

Market segmentation, then, consists of dividing a diverse market into a number of smaller, more similar, sub-markets. The objective is to identify groups of consumers with similar requirements so that they can be served effectively while being of a sufficient size for the product or service to be supplied efficiently.[72] A market can be segmented in a variety of ways. It can be geographical factors, such as different regions or climate, demographical factors, like age or gender, psycho graphical factors, such as lifestyle and personality, or behavioral factors, for example purchase occasion or benefit sought.[73] Each segment should consist of

[65] Stokes, D., 2000, p. 51
[66] Landström, H. & Löwegren, M. (eds.), 2009, p. 154
[67] McQuarrie, E., 2006, p. 3
[68] Andberg, L. & Eliasson, B., 2005, p. 11
[69] Armstrong, G., Kotler, P., Saunders, J. & Wong, V., 2005, p. 391
[70] Armstrong, G., Kotler, P., Saunders, J. & Wong, V., 2005, p. 31
[71] Jobber, D., 2007, p. 275
[72] Jobber, D., 2007, p. 275
[73] Armstrong, G., Kotler, P., Saunders, J. & Wong, V., 2005, p. 399

customers with similar needs and behavior and thereby differentiate themselves from other individuals or groups of customers.[74]

The company should then evaluate the attractiveness of each market segment and selecting one or more segments to enter, this is called *market targeting,* i.e. to practice segmentation.[75] An organization evaluates its strengths relative to the competition and considers how many segments it can serve effectively.[76] The company should select those segments where they can offer the most.[77]

3.2 SWOT Analysis

To evaluate the product of SPAGO Imaging AB, a SWOT analysis has been conducted. A SWOT analysis is a structured approach to evaluating the strategic position of a business by identifying its strengths (S), weaknesses (W), opportunities (O) and threats (T).The aim is to identify the internal strengths and weaknesses of an organization and to consider if they are adequate to handle the external opportunities and threats that exist around the company.[78] If the analysis is used correctly it can help the manager anticipate important developments that can have an impact on the company.[79]

	Helpful	**Harmful**
Internal	Strengths	Weaknesses
External	Opportunities	Threats

Table 3.1 – Strengths, weaknesses, opportunities and threats (SWOT) analysis.

[74] Landström, H. & Löwegren, M. (eds.), 2009, p. 157
[75] Ries, A. & Trout, J., 1985, p. 13
[76] Armstrong, G., Kotler, P., Saunders, J. & Wong, V., 2005, p. 31
[77] Kotler, P., 1999, p. 48
[78] Jobber, D., 2007, p. 47
[79] Armstrong, G., Kotler, P., Saunders, J. & Wong, V., 2005, p. 58

When evaluating strengths and weaknesses, only those resources or capabilities that a customer would value should be included.[80] The strengths and weaknesses in the analysis should be based on facts and be relative, not absolute.[81]

The opportunities and threats that are listed should be events or trends outside the business that have implications for performance.[82] Not all threats call for the same attention. It is important to assess the likelihood of each threat and the potential damage each case could cause and then focus on the most probable and harmful threats and prepare plans to meet them.[83] Opportunities often involves risks, so when evaluating opportunities, the manager must decide whether the expected returns justify these risks.[84]

3.3 Product Life Cycle

The product life cycle (PLC) is a curve which breaks down product sales into four stages. The stages are *introduction, growth, maturity* and *decline*, see Figure 3.1.[85] The curve is shaped like an S and reflects a process of slow adoption in the early stages, followed by a rapid acceleration and ending with a plateau representing the limited demand.[86]

The product life cycle concept is useful for management in several ways; one way is to conceptualize different general approaches to developing core strategies. It is a quite flexible tool and can be applied to both brands and product lines.[87] Each stage represents specific challenges, therefore can particular strategies be found on each stage.[88]

[80] Piercy, N., 2002, p. 259
[81] Armstrong, G., Kotler, P., Saunders, J. & Wong, V., 2005, p. 59
[82] Jobber, D., 2007, p. 48
[83] Armstrong, G., Kotler, P., Saunders, J. & Wong, V., 2005, p. 58
[84] Armstrong, G., Kotler, P., Saunders, J. & Wong, V., 2005, p. 58
[85] Jobber, D., 2007, p. 386
[86] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 333
[87] Jobber, D., 2007, p. 386
[88] Jobber, D., 2007, p. 388

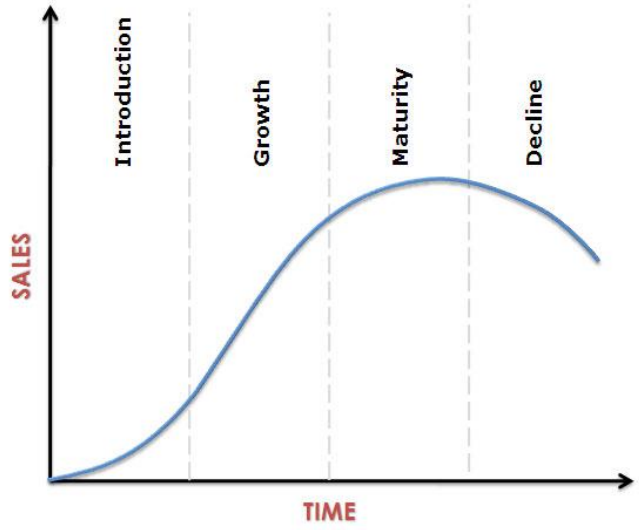


Figure 3.1 – The Product Life Cycle.[89]

Introduction **-** When a product is first introduced on the market both the growth rate and the size of the market is low.[90] The introduction phase is also characterized by few (or no) competitors. The sales volume increases slowly due to the small number of firms marketing the product and the reluctance of the customers.[91]

The objective for a product in the introduction stage is to build sales by expanding the market for the product. It is important to create product awareness so that more customers will become familiar with the benefits of the product. The product is likely to be non-differentiated to appeal to different customer groups.[92]

There are two well-known strategy options in the introduction phase: *skimming* or *penetrating*. The skimming strategy assumes a product feature-based advantage that allows the company to enter the market with a high price. Target customers are the least price sensitive. The company should choose a skimming strategy when the cost structure of the product is largely variable cost, which is usually the case with manufactured goods. The skimming strategy is also the best choice when high entry barriers exist, because high prices make the market very attractive to potential competitors. A penetration strategy is just the opposite:

[89] Homepage of NoteDesk, *The product life cycle* [Online]
[90] Lehmann, D. & Winer, R., 2005, p. 54
[91] Lehmann, D. & Winer, R., 2005, p. 236
[92] Jobber, D., 2007, p. 389

the company uses a low-price strategy to attempts to get as many customers as quickly as possible. A penetration strategy should be chosen if the fixed costs are high or the product is assumed to be short-lived.[93]

Growth **-** Growth is a stage characterized by a period of faster sales and profit growth. The growth is fuelled by rapid market acceptance and sometimes also repeat purchasing. Profits may begin to decline in the end of the stage as new rivals enter the market, attracted by the high profit potential. As customers become more knowledgeable about the available products, this puts pressure on the prices.[94]

The objective during the growth phase is to both increase sales and gain higher market share. To accomplish this task the product is often redesigned to create differentiation.[95] Another key focus should be to try hold on to the distribution channels.[96]

The starting point of the growth phase is sometimes referred to as the *tipping point*. In the tipping point the demand for the product suddenly takes off, with explosive growth. There is therefore very important to try to anticipate when the tipping point will occur, otherwise it leads to missed sales and easy opportunities for competitors.[97]

Maturity **-** The maturity stage is a period where saturation occurs. The market is not growing and the existing competitors are fighting for market share.[98]

The objective should be to hold on to profits by protecting the existing market share rather than try to increase the sales.[99] There is a need for effective brand building as brand leaders are in the strongest position to resist the pressure on profit margins.[100]

[93] Lehmann, D. & Winer, R., 2005, p. 237
[94] Jobber, D., 2007, p. 387
[95] Jobber, D., 2007, p. 389
[96] Lehmann, D. & Winer, R., 2005, p. 238
[97] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 334
[98] Jobber, D., 2007, p. 388
[99] Jobber, D., 2007, p. 390
[100] Jobber, D., 2007, p. 388

Decline **-** The last stage is decline, where the demand for the product is reduced so the sales and profits fall.[101]

The conventional strategies in the decline stage are either *harvest* or *divest*. The harvest strategy would result in higher prices in an effort to boost profit margins. The divestment strategy may take the form of selling products to other companies or simply product elimination.[102] There is also a strategy to try to be the last in the market. By being last, the product can have monopoly to the few customers left and to charge these customers with high prices.[103]

3.4 The Ansoff Product/Market Growth Matrix

To better understand the challenges witch the product faces, the *Ansoff product /market growth matrix* is a useful tool. The Ansoff product/market growth matrix provides a simple way of generating four basic alternative directions for strategic development, see Figure 3.2. The matrix considers four growth options: *market penetration, product development, market development* and *diversification*.[104]

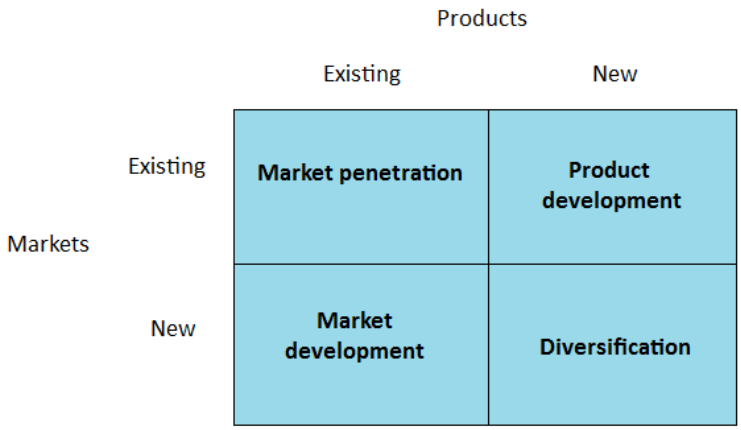


Figure 3.2 – The Ansoff product /market growth matrix.

[101] Jobber, D., 2007, p. 388
[102] Jobber, D., 2007, p. 391
[103] Lehmann, D. & Winer, R., 2005, pp. 239-240
[104] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 257

Market penetration - Market penetration is a strategy where existing product is launched on an already existing market. The aim is to gain market share.[105] The most basic method of gaining market penetration is by winning competitors´ customers. Another way of gaining market penetration is to buy the competitors.[106]

Companies that choose the market penetrating strategy may face legal constrains because greater market share can raise concerns from official competition regulators.[107] A market penetration strategy can also exacerbate the industry rivalry as other competitors in the market defend their share. Increased rivalry can lead to price wars or expensive marketing battles, which may cost more than any market share gains are actually worth. If retaliation is a danger, the company needs strategic capabilities that give a clear competitive advantage.[108] The dangers of provoking fierce retaliation are greater in low-growth markers, as any gains in volume will be much more at the expense of other players.[109] In low-growth or declining markets, it can therefore be more effective to buy the competitors. By decreasing the number of independent players, buying the competitors can actually reduce the rivalry. [110]

Product development - Product development is when the company delivers new products to existing markets.[111] There are three different ways of doing a product development: *product extension*, *product replacement* or *product innovation*. Product extension is when the company extends the existing product lines to give current customers greater choices. New features are added to enhance the value of the products.[112] Product replacement is when old models or brands are replaced with new ones. The final option to a product development strategy is innovation; to replace an old product with a fundamentally different one. The new product is often based on a new technology.[113]

Generally, there are two common approaches for innovation: *technology push* or *market pull*. In technology push the scientists create new knowledge, which form

[105] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 258
[106] Jobber, D., 2007, p. 405
[107] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 260
[108] Johnson, G., Scholes, K. & Whittington, R., 2008, pp. 258-259
[109] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 258
[110] Johnson, G., Scholes, K. & Whittington, R., 2008, pp. 259-260
[111] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 261
[112] Jobber, D., 2007, p. 406
[113] Jobber, D., 2007, p. 407

the basis for new products. The new products are then "pushed" to the customers.[114] Therefore, it does not matter if a certain demand already exists or not.[115] Market pull is instead when the customers is responsible for the innovation.[116] The source for the innovation is an inadequate satisfaction of customer needs, which results in new demands for problem-solving.[117]

Market development **-** Market development is where companies deliver existing products to new markets, i.e. new users or new geographies. The major challenge is to coordinate between different segments which might all have different needs.[118] The risk of product development is that it can lead to saturation of existing market segments.

Diversification **-** Diversification is a strategy where the company launches a new product on a new market.[119] If a company has underutilized resources or competences it can use these for diversification into new activity.[120] Another common justification for the diversification strategy is to spreading the risk. The diversification can be *related* or *unrelated*. Related diversification is a product development beyond current products and markets, but within the capabilities of the company. An unrelated diversification is just the opposite, a development of products beyond the current capabilities.[121]

[114] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 326
[115] Brem, A. & Voigt, K.-I., 2009, p. 355
[116] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 326
[117] Brem, A. & Voigt, K.-I., 2009, p. 355
[118] Johnson, G., Scholes, K. & Whittington, R., 2008, pp. 261-262
[119] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 262
[120] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 263
[121] Johnson, G., Scholes, K. & Whittington, R., 2008, p. 265

4. Empirics: Cancer and Methods for Cancer Detection

Chapter four contains information about cancer, breast cancer, as well as current techniques to detect breast cancer.

4.1 Cancer

"Cancer represents a tremendous burden on patients, families, and societies. It is one of the leading causes of death in the world and is still increasing, particularly in developing countries. Almost seven million people die each year of cancer, and many of these deaths can be avoided if appropriate measures are put in place to prevent, early detect, cure and care…."[122]

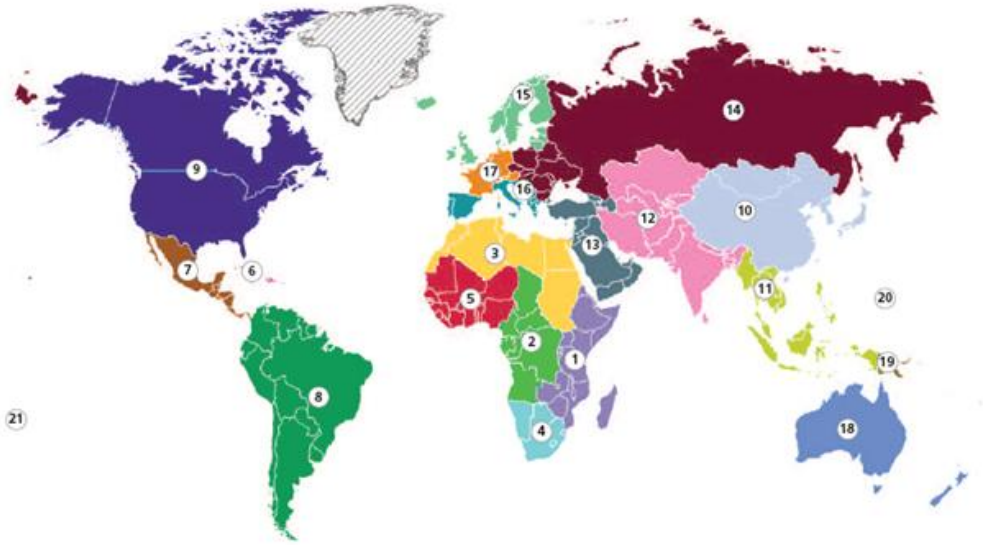
- Dr LEE Jong-Wook, Director-General, WHO

Cancer is not a single disease but a group of diseases of which there are over a hundred types.[123] The disease is characterized by uncontrolled growth and spread of abnormal cells. It can be classified into two types: *hematological* (malignancies of the blood) or *solid tumors*.[124] If the tumors are spreading, they are referred to as *malignant* tumors, i.e. cancer is present. There are also tumors that are not cancerous, known as *benign*. Benign tumors are growing slowly, they do not spread and they are rarely life-threatening.[125]

More than 11 million people are diagnosed with cancer every year and it is estimated that there will be 16 million new cases per year by the year 2020.[126] Cancer is the second leading cause of death in economically developed countries, following heart diseases, and the disease are becoming more common also for the less developed countries. Already half of all cancer cases occur in developing countries.[127]

[122] World Health Organization & International Union Against Cancer, 2005, p. 2
[123] Zebrowski, M., 2007, p. 19
[124] Zebrowski, M., 2007, p. 19
[125] Nystrand, A (ed.), 2005, p. 6
[126] Hayat, M. (ed.), 2008, p. xvii
[127] Center, M., Garcia, M., Hao, Y., Jemal, A., Siegel, R., Thun, M. & Ward, E., 2007, p. 1

Figure 4.1 shows the estimated number of new cancer cases in the year of 2007 sorted by geographical area.



1. Eastern Africa (290,100)
2. Middle Africa (87,800)
3. Northern Africa (142,100)
4. Southern Africa (78,100)
5. Western Africa (166,300)
6. Caribbean (73,500)
7. Central America (184,800)
8. South America (733,100)
9. North America (1,745,400)
10. Eastern Asia (3,313,600)
11. South-Eastern Asia (618,800)
12. Central Asia (1,451,700)
13. Western Asia (225,900)
14. Eastern Europe (939,500)
15. Northern Europe (448,700)
16. Southern Europe (675,000)
17. Western Europe (950,500)
18. Australia (117,700)
19. Melanesia (7,700)
20. Micronesia (700)
21. Polynesia (900)

Figure 4.1 – Estimated number of New Cancer Cases by World Area, 2007.[128]

The number of deaths caused by cancer is constantly increasing, with an expected rise by 45% from 2007 to 2030, from 7.9 million to 11.5 million deaths. This is due largely to an increase in both population and life expectancy.[129]

[128] Center, M., Garcia, M., Hao, Y., Jemal, A., Siegel, R., Thun, M. & Ward, E., 2007, p. front page
[129] Loncar, D. & Mathers, C., 2006, p. 2017

Cancer is about as common among men as among women, but men and women are affected by various forms of cancer.[130] As seen in Figure 4.2, the most commonly diagnosed cancers for men are *lung- & bronchus*, *prostate* and *stomach cancer*, and for women it´s *breast*, *cervix uteri* and *colon- & rectum cancer*.[131]

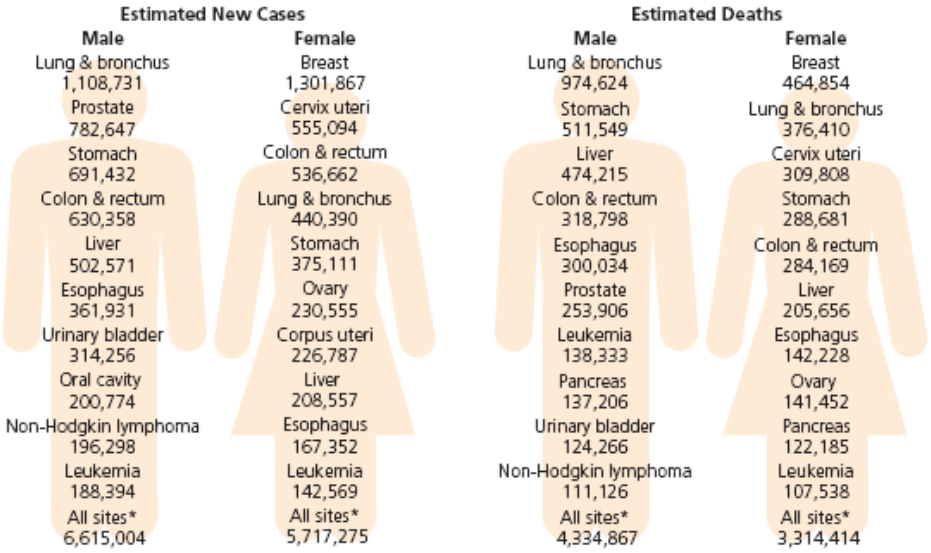


Figure 4.2 – Estimated new cancer cases and deaths worldwide year 2007.[132]

There are many causes of cancer and often a variety of factors interact in a complicated way for cancer to occur. There are different risk factors that contribute to causing cancer, both external and internal factors. Examples of external factors are tobacco, chemicals, radiation and infectious organisms. Some examples of internal factors are inherited mutations, different hormones, immune conditions and mutations.[133] Depending on type and stage of the disease, cancer can be treated by surgery, radiation therapy, hormone therapy, biological therapy or chemotherapy.[134]

[130] Nystrand, A (ed.), 2005, p. 6
[131] Center, M., Garcia, M., Hao, Y., Jemal, A., Siegel, R., Thun, M. & Ward, E., 2007, pp. 1-2
[132] Center, M., Garcia, M., Hao, Y., Jemal, A., Siegel, R., Thun, M. & Ward, E., 2007, p. 3
[133] American Cancer Society, 2008, p. 1
[134] American Cancer Society, 2008, p. 1

4.1.1 Breast Cancer

Breast cancer represents a major public health problem, with over 1 million new cases each year.[135] Table 4.1 shows the number of new breast cancer cases and the prevalence (the total number of cases) the year 2006 in some of the most affected countries.

Country	New Incidences 2006	Prevalence 2006
France	42907	199746
Germany	55366	236736
Italy	37053	No information found
Spain	16047	73242
UK	41664	164963
Japan	33215	152593
USA	223543	1049964
Sweden[136]	7096	No information found

Table 4.1 – New incidences and prevalence of breast cancer across the seven major markets, 2006.[137]

Death rates from breast cancer have been steadily decreasing due to a combination of early detection and improved treatment. Nevertheless, 40-60% of all patients diagnosed with breast cancer will die from the disease.[138] At stage 0, also referred to as *Ductal Carcinoma In Situ* (DCIS), which is defined by the absence of invasion of surrounding tissues, the five-year survival rate is 100%, but for women with stage IV (cancer has spread beyond the breast) its only 16%.[139] Considering these facts, it is apparent that more effective methods for early detection of this malignancy are urgently needed.

A female breast consists of a number of milk glands where the breast milk is formed. Each gland has a milk *duct*, a passage that leading the milk to the nipple. The rest of the breast is made up by fat and connective tissue. In most cases breast cancer begins in the ducts, but it can also originate from milk glands or from connective tissue cells.[140]

[135] Center, M., Garcia, M., Hao, Y., Jemal, A., Siegel, R., Thun, M. & Ward, E., 2007, p. 3
[136] Socialstyrelsen, 2007, p. 19
[137] Zebrowski, M., 2007, p. 35
[138] Bruening, W., Kostinsky, H., Launders, J., Pinkney, N., Schoelles, K. & Turkelson, C., 2006, p. 5
[139] American Cancer Society, 2007, p. 1
[140] Nystrand, A (ed.), 2005, p. 36

The cause of breast cancer is unknown, but researchers have found a number of potential risk factors for breast cancer. These can be divided into seven categories: *age*, *family history of breast cancer*, *hormonal factors*, *proliferative breast disease*, *radiation of the breast region*, *personal history of malignancy* and *lifestyle factors*.

Age **-** Increasing age is the single most important risk factor for developing breast cancer.[141] The age-specific probabilities of developing breast cancer are shown in Table 4.2.

Age-specific Probabilities of Developing Breast Cancer	
Current age	**Probability of developing breast cancer in the next 10 years [%]**
20	0.05
30	0.44
40	1.46
50	2.73
60	3.82
70	4.14

Table 4.2 – Age-specific probabilities of developing breast cancer. (The information is based on cases diagnoses 2000-2002.)[142]

Though the risk for having breast cancer rises with age, it is important to know that the breast cancer tends to be more aggressive when it occurs in younger women.[143]

Family history **-** 5–10% of all breast cancer cases result from inherited mutations in breast cancer susceptibility genes, such as BRCA1 and BRCA2.[144] Women with a family history of breast cancer therefore have an increased risk of developing breast cancer themselves. If a first-degree relative (i.e., mother, sister or daughter) have a history of breast cancer the relative risk is 1.8 times higher than it would be otherwise.[145]

[141] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 31
[142] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 32
[143] Zebrowski, M., 2007, p. 33
[144] American Cancer Society, 2009, p. 9
[145] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 32

Hormonal factors **-** Early menarche (before 12 years of age), late menopause (after 55 years of age) and late age at first full-term pregnancy (35 years or older) increase a woman's risk of breast cancer by affecting the reproductive hormones.[146] Exogenous hormones, for example birth control pills, have also been linked to increase the breast cancer risk. Findings from an analysis done by the Collaborative Group (1996) showed that women who use birth control pills had a slightly increased risk of developing breast cancer.[147] In contrast, a more recent finding from the Women's Contraceptive and Reproductive Experiences trial (2002) indicated that users of birth control pills did not have an increased risk of developing breast cancer.[148]

Proliferative Breast Disease **-** Some women with a history of abnormal breast tissue have an increased risk for developing breast cancer. The degree of increase in risk depends on the specific epithelial abnormality.[149]

Radiation of the Breast Region at an Early Age **-** Radiation of the breast during early age (before 30 years) increases the risk of breast cancer. The greatest risk is seen in individuals exposed to radiation before age 15; some studies suggest as great as a 35% increased risk of breast cancer in such individuals by the age 40.[150]

Personal History of Malignancy **-** A personal history of breast cancer increases the risk of a subsequent breast cancer. Personal history of other malignancy, such as endometrial, ovarian or colon cancer, may also increase the risk of developing breast cancer.[151]

Lifestyle Factors **–** Several lifestyle factors play a significant role in determine an individual´s risk of breast cancer, for example diets with high fat and red meat content. Also high alcoholic consumption leads to increased risk for developing breast cancer.[152] A recent study published in the Journal of Cancer Epidemiology (2009) has proved that being overweight also leading to an increased risk for

[146] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 32
[147] Collaborative Group on Hormonal Factors in Breast Cancer, 1996, p. 1713
[148] Berlin, J., Bernstein, L., Burkman, R., Daling, J., Folger, S., Malone, K., Mandel, M., Marchbanks, P., McDonald, J., Norman, S., Simon, M., Spirtas, R., Strom, B., Ursin, G., Weiss, L., Wilson, H. & Wingo, P., 2002, p. 2025
[149] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 35
[150] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 35
[151] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, pp. 35-36
[152] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 36

breast cancer. The risk depends on how late in life the weight gain occurs, for example a women who gains more than 10 kilo after age 30 or more than 5.5 kilos after age 40, has almost twice the risk to develop breast cancer as a women whose weight is stable. The research teams also found that smoking a pack of cigarettes a day for nine years increases breast cancer risks by 59%.[153]

The earliest sign of breast cancer is often an abnormality detected on a mammogram screening or a lump felt by the woman or health care professional. Other, less common, symptoms are persistent changes to the breast such as thickening, swelling, distortion, tenderness, skin irritation and redness, or nipple abnormalities such as ulceration, retraction and spontaneous discharge.[154]

How the cancer should be treated depends on the stage and biological characteristics of the cancer, as well as the patient's own preferences.[155] Most patients will have some type of surgery, often combined with other treatments such as radiation therapy, chemotherapy, hormone therapy or biologic therapy. The primary goal of breast cancer surgery is to remove the cancer from the breast and to assess the stage of disease. There is two way of conducting a surgery, either by *mastectomy* or *lumpectomy*. In a mastectomy the entire breast is removed and in a lumpectomy, only the tumor plus a rim of normal tissue is removed. Lumpectomy is almost always followed by about five to seven weeks of radiation therapy.[156] Radiation is used to destroy cancer cells remaining in the breast, chest wall or underarm area after surgery. It could also be used to reduce the size of a tumor before surgery.[157] A woman who chooses lumpectomy and radiation will have the same expected long-term survival as if she had chosen mastectomy.[158]

Since the cause of the disease remains unknown, early detection and diagnosis is the key for breast cancer control. It can increase the probability of successful treatment, save lives and reduce costs.

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[153] Bissonauth, V., Fafard, E., Ghadirian, P., Maugard, C., Narod, S., Robidoux, A. & Shatenstein, B., 2009, p. 6
[154] American Cancer Society, 2008, p. 9
[155] American Cancer Society and National Comprehensive Cancer Network, 2006, p. 6
[156] American Cancer Society, 2007, pp. 17-18
[157] Early Breast Cancer Trialists' Collaborative Group, 2000, p. 1757
[158] Anderson, S., Bryant, J., Deutsch, M., Fisher, B., Fisher, E., Leong, J.-H., Margolese, R. & Wolmark, N., 2002, p. 1233

4.2 Current Techniques for Breast Cancer Detection

Segmentation of the different techniques has been done to better organize the empirical data. The techniques have been divided into two segments depending on the users' different needs. The segments are *screening tests* and *diagnostic tests*.

Segment	Tests
Screening tests	Mammography Magnetic Resonance Imaging (MRI) Sonography Breast Physical Examination (BPE) Breast Self-Examination (BSE) Ductal Lavage (DL) Thermography
Diagnostic tests	Biopsy Magnetic Resonance Imaging (MRI) Tumor Marker Test Mammography Sonography Nuclear Medicine Breast Imaging Computerized Tomography (CT) Positron Emission Tomography (PET)

Table 4.3 – The segmentation of the different technologies for breast cancer detection.

Screening tests **-** Because early breast cancer is asymptomatic, the only way to detect it is through screening. Screening tests are given routinely to people who appear to be healthy and are not suspected of having breast cancer. The goal of this type of tests is to identify all individuals who might have breast cancer.

One subgroup of the screening patients is women who have a higher risk for developing breast cancer. These are referred to as *risk group screening*. Women at high risk include those who:[159]

• Have a known BRCA1 or BRCA2 gene mutation.

• Have a first-degree relative with a BRCA1 or BRCA2 gene mutation.

• Have a lifetime risk of breast cancer of 20%-25% or greater, according to risk assessment tools that are based mainly on family history.

[159] American Cancer Society, 2007, pp. 13-14

• Had radiation therapy to the chest when they were between the ages of 10 and 30 years.

• Have Li-Fraumeni syndrome, Cowden syndrome or Bannayan-Riley-Ruvalcaba syndrome, or have a first-degree relative with one of these syndromes.

• Have a personal history of breast cancer.

The screening tests are: *Mammography, Magnetic Resonance Imaging (MRI), Sonography, Breast Physical Examination (BPE), Breast Self-Examination (BSE), Ductal Lavage (DL)* and *Thermography.*

Diagnostic tests **-** Diagnostic tests are given to people who are suspected of having breast cancer, either because of symptoms they may be experiencing or after abnormal findings in screening test. These tests are used to determine whether or not breast cancer is present and, if so, whether or not it has traveled outside the breast. Diagnostic tests also are used to gather more information about the cancer, for example the location and the size of the tumor, to guide decisions about treatment.

Once breast cancer is diagnosed, tests are used during and after treatment to monitor how well therapies are working. These tests is often referred to as *monitoring tests*, but because both the tests and the need they satisfy is the same as the diagnostic tests, will these tests also be referred to as diagnostic tests.

The diagnostic tests are: *Biopsy, Magnetic Resonance Imaging (MRI), Tumor Marker Test, Mammography, Sonography, Nuclear Medicine Breast Imaging, Computerized Tomography (CT)* and *Positron Emission Tomography (PET).*

Two important concepts most be defined before the different techniques are presented: *sensitivity* and *specificity*. The sensitivity represents the proportion of truly diseased persons in a population who are identified as being diseased by the test. It is a measure of the probability of correctly diagnosing a condition.[160] Specificity of a test is defined as the percentage of persons without the disease of

[160] Last, J., Porta, M., 2008, p. 227

interest who have negative test results. It is a measure of the probability of correctly identifying a non-diseased person.[161] A more detailed explanation of the two concepts can be found in Appendix B.

A complementary analysis of future techniques, which are under various stages of research and development, has also been conducted and is presented in Appendix C.

4.2.1 Screening Tests

Mammography

Mammography is an x-ray method for evaluation of breast tissue. The first mammography unit was introduced in 1965, and ever since then, mammography screening trials and programs for detecting breast cancer have been organized all around the world.[162] Today mammography is the most widely used imaging modality for early detection of breast cancer.[163]

In mammography, the breasts are compressed between two plates while a special camera takes pictures of the breasts.[164, 165] Tumors are detected on the basis of differences in x-ray attenuation, distortions in tissue architecture or appearance of certain patterns of micro calcifications (tiny specks of calcium in the breast).[166]

Mammography can be done in *standard* or in *digital* form. In standard mammography, images are recorded on film using an x-ray cassette. The film is then viewed by the radiologist using a light box. In digital mammography, the breast image is captured using a special electronic x-ray detector, which converts the image into a digital picture for review on a computer monitor. Digital mammography uses the same mammographic system as conventional mammography, but the system is equipped with a digital receptor instead of a film cassette.[167] The digital mammography has an advantage that the systems offer opportunities for post-processing and reconfiguring of the original data.[168]

[161] Last, J., Porta, M., 2008, p. 227
[162] Boné, B., 1997, pp. 1-2
[163] Maggi, C., Messineo, D., Potente, G. & Savelli, S., 2009, p. 83
[164] Homepage of Breastcancer.org, *Mammograms* [Online]
[165] Homepage of Breastcancer.org, *Mammograms* [Online]
[166] Hylton, N., 2005, p. 1678
[167] Homepage of Imaginis, *Digital Mammography* [Online]
[168] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 84

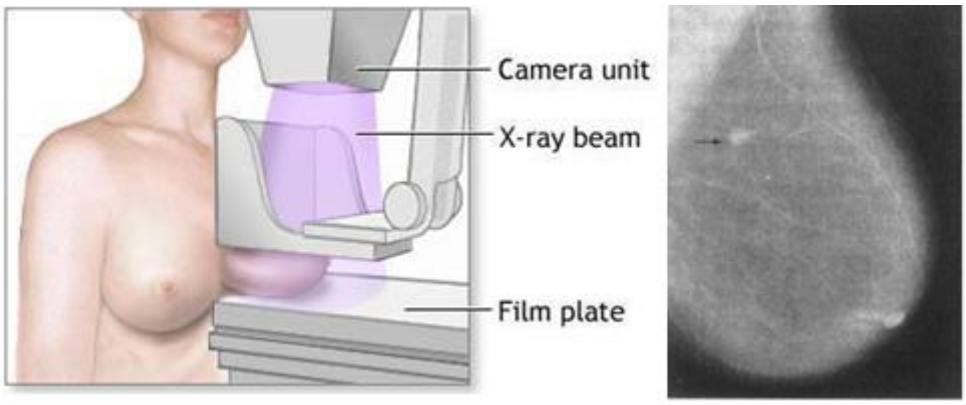

Figure 4.3 – The mammography equipment and a mammogram of a breast. The arrow shows a high-density, irregular mass that indicate cancer.[169, 170]

Leading experts in the U.S. such as the American Cancer Society (ACS), the American College of Radiology (ACR) and the National Cancer Institute (NCI) recommend annual mammograms for women over 40.[171] The Swedish authority Socialstyrelsen, recommend mammograms for women 40-74 year, with 18-months intervals for women 40-54 year and 2-years intervals for women age 55-74 year.[172] The specificity of mammography is 95.7% and the sensitivity is 79%.[173] The cost of a mammogram is $150 to $200 per scan.[174]

In mammography x-rays are used, which are photons with higher energy levels than visible light. This radiation, which is powerful enough to knock electrons from atoms, is known as *ionizing radiation.* Because the body absorbs some of the ionizing radiation used in mammography, the radiation can cause damage at the molecular level and produce adverse health effects.[175] The radiation dose received during a screening mammogram is about the same amount of radiation a person gets from the natural surroundings in an average 3-month period (0.7 mSv).[176]

[169] Homepage of The New York Times, *Mammography* [Online]
[170] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 87
[171] Homepage of Breastcancer.org, Mammography: Benefits, Risks, What You Need to Know [Online]
[172] Homepage of Praktiskmedicin, *Rekommendationer* [Online]
[173] Abraham, L., Aiello Bowles, E., Carney, P., Elmore, J., Miglioretti, D., Sickles, E., & Yankaskas, B., 2008**,** p. 1200
[174] Sayewitz, R., 2002, Jupiter Medical buys digital mammography machine, South Florida Business Journal [Online]
[175] Masha, Z., 2002, p. 3
[176] Homepage of Breastcancer.org, Mammography Technique and Types [Online]

Several studies have been done to evaluate mammography as a screening test, i.e. Shapiro et al. (1988), Mettlin & Smart (1994), Tabar et al. (1995), Andersson & Janzon (1997), Hendrick et al. (1997), Smart et al. (1997) and Feig et al. (1998). These studies showed that screening mammography in women aged 40 years and older reduces cancer deaths by 29 to 45%.[177] In contrast, a more recent study done by Gøtzsche & Olsen (2000), found no reduction in mortality with mammography, so the authors concluded that screening for breast cancer with mammography is unjustified.[178]

It is difficult to interpret mammography for young women because their breasts tend to be dense and full of milk glands.[179] The sensitivity of standard mammography in dense breast is therefore only 30 to 48%.[180] Digital mammography is somewhat more sensitive in women with dense breasts, but outcome studies are lacking.[181] In addition, some literature has evaluated the relationship between breast density and the risk of developing cancer. Two specific studies of 237 and 622 women each concluded that the risk of breast cancer is increased 2.2- to 5-fold in patients with dense breasts compared with those with fatty breasts.[182, 183] Another area where mammography is of limited value is in the examination of breasts containing implants.[184]

Mammography can also be uncomfortable or even painful for some women, because the breast is compressed to flatten and reduce the thickness of the breast.[185] This pain makes some women avoid this potentially life-saving screening procedure.[186]

According to the American Cancer Society, about 10% of women who have a mammogram will require more screening tests. [187]

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[177] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 85
[178] Gøtzsche, P. & Olsen, O., 2000, p. 129
[179] Homepage of Breastcancer.org, Ultrasound [Online]
[180] Allison, K., De Paredes, E. & Smith, M., 2006, p. 311
[181] Knutson, D. & Steiner, E., 2007, p. 1663
[182] Kashiki, Y., Kawaguchi, Y., Nagao, Y., Saji, S. & Sugiyama Y, 2003, p. 228
[183] Astrahan, M., Bernstein, L., Ma, H., Parisky, Y., Pike, M., Salane, M., Siozon, C., Ursin, G. & Wu, A., 2003, p. 335
[184] Changlassian, T. & Dershaw, D., 1989, p. 69
[185] Homepage of Breastcancer.org, *Mammography Technique and Types* [Online]
[186] Homepage of National Institute of Biomedical Imaging and Bioengineering (NBIB), *Dedicated Breast CT Scanner Offers Alternative to Mammography* [Online]
[187] Homepage of Breastcancer.org, *Mammography: Benefits, Risks, What You Need to Know* [Online]

Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging is based on the discovery of Nuclear Magnetic Resonance (NMR). NMR is a physical phenomenon that was discovered by two American research teams, Bloch et al. and Pound et al., in 1946. They found, independently of each other, that when certain nuclei were placed in a magnetic field they absorbed energy in the radiofrequency range and re-emitted this energy during the transition to their original orientation. The technique was referred to as Nuclear Magnetic Resonance.[188, 189] However, as the word *nuclear* was associated in the public mind with nuclear warfare, the adjective nuclear was dropped when the method was introduced to clinical practice in the early 1980s.[190]

MRI uses a static magnetic field (commonly between 0.5-3 Tesla) to align the nuclear magnetization of hydrogen atoms in water. Radio frequency pulses are used to systematically alter the alignment of this magnetization, causing the hydrogen nuclei to absorb and then re-emit the energy in a way that reveals information about the physical and chemical properties of the tissue´s environment in the body. For better contrast, patients get contrast agents injected. These agents enhance the tissue contrast by increasing the brightness in various parts of the body where the agent resides. The most common contrast media used today is made up of individual atoms of gadolinium, which are held tightly by a non-toxic small molecule, to prevent toxic effects.[191, 192]

[188] Bloch, F., Hanson, W. & Packard, M., 1946, p. 127
[189] Pound, R., Purcell, E. & Torrey, H., 1946, pp. 37-38
[190] Rinck, P., 2003, p. 2
[191] Rinck, P., 2003, p. 5
[192] Rinck, P., 2003, p. 149

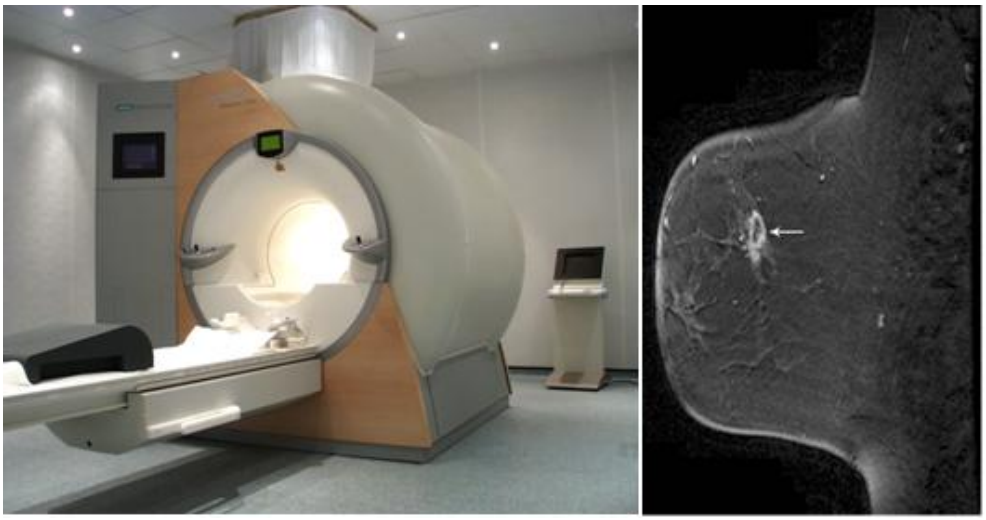

Figure 4.4 – The MRI equipment and an MRI picture, there the arrow points to a high-density, irregular mass that indicate cancer.[193, 194]

American Cancer Society is not recommending MRI for screening women at average risk of breast cancer, but they recommend annual screening with MRI for women with high risk, so called risk group screening.[195] The specificity of MRI (conducted with current contrast agents) is 72.4% and the sensitivity is 92.5%.[196] The cost of an MRI examination is $1,000 to $1,500 per scan.[197]

MRI uses radio-frequency waves, which are photons with energy levels lower than visible light. This low-energy radiation is *non-ionizing* and is considered much safer than ionizing radiation.[198] MRI has no limitations in terms of detecting cancer in dense breasts or in breasts with implants.[199]

One in ten women diagnosed with cancer in one breast will develop the disease in the opposite breast, the *contralateral* breast.[200] Liberman et al. (2003) performed

[193] Homepage of Modular Healthcare Facilities, *MRI picture* [Online]
[194] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 113
[195] Andrews, K., Boetes, C., Burke, W., Harms, S., Leach, M., Lehman, C., Morris, E., Pisano, E., Russell, C., Saslow, D., Schnall, M., Sener, S., Smith, R., Warner, E. & Yaffe, M., 2007, p. 76
[196] Bruening, W., Kostinsky, H., Launders, J., Pinkney, N., Schoelles, K. & Turkelson, C., 2006, p. 67
[197] Sayewitz, R., 2002, *Jupiter Medical buys digital mammography machine*, South Florida Business Journal [Online]
[198] Masha, Z., 2002, p. 3
[199] Aspelin, P., Boné, B., Isberg, B., Perbeck, L. & Veress, B., 1995, p. 111
[200] Fox, M., 2007, New recommendations call for MRI in breast cancer, Published on Breastcancer.org [Online]

a study that included 223 women with known breast cancer who underwent MRI of a mammographically normal contralateral breast. Cancer was detected by MRI in 12 women (5%).[201] Based on the results of this and other studies, the American Cancer Society now recommends that women diagnosed with cancer in one breast have an MRI scan of the contralateral breast.[202]

The presence of micro calcifications is a strong indication that Ductal Carcinoma In Situ (DCIS) is present. Breast MRI can´t detect micro calcifications because the calcium don´t give any signals.[203] However, a study done by Kuhl et al. showed that MRI was better than mammography at finding DCIS. About 90% percent of DCIS was found by MRI, while only 56% was found by a mammogram[204] On the other hand, small foci of DCIS (less than 3 mm in diameter) was often missed on MRI and the extent of DCIS is overestimated by MRI in 50% of cases.[205, 206]

Sonography

Sonography of the breast, also called breast ultrasound, is a sound based imaging modality and was first described in 1952 by Wild & Reid.[207] The scanners consist of a console containing a computer, a display screen and a transducer, a small hand-held device that resembles a microphone attached to the scanner by a cord. The transducer sends out high frequency sound waves into the body and then listens for the returning echoes. The image is created based on the amplitude (strength), frequency and the time it takes for the sound to return from the patient to the transducer.[208]

[201] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 112
[202] Fox, M., 2007, New recommendations call for MRI in breast cancer, Published on Breastcancer.org [Online]
[203] Hylton, N, 2005, p. 1679
[204] Bieling, H., Huhn, W., Koenig, R., Kuhl, C., Leutner, C., Schild, H., Schrading, S. & Wardelmann, E., 2007, p. 485
[205] Berg, W., Bhargavan, M., Carter, B., Gutierrez, L., Ioffe, O., Lewis, R. & NessAiver, M., 2004, p. 830
[206] Berg, W., 2001, p. 153
[207] Boné, B. 1997, pp. 2-3
[208] Homepage of RadiologyInfo, *Breast Ultrasound* [Online]

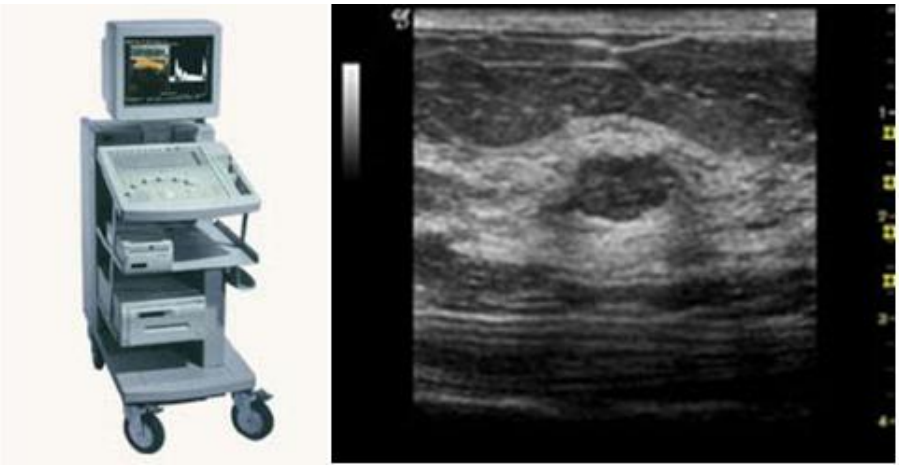

Figure 4.5 – The Sonography equipment and a Sonography image that show a cluster of small calcifications that may indicate that cancer is present.[209,210]

Sonography is not recommended to any major group as a screening tool; it is only used to complement other screening tests.[211] The sensitivity is 86.1% and the specificity 66.4%.[212] The cost of a sonography examination is $150.[213]

Sonography involves no radiation, only harmless sound waves. The method has no limitation in dense breasts, but it is technically difficult to interpret the method in women with large breasts.[214, 215]

According to a study published in European Radiology, the detection rate doubled when Sonography and mammography were combined compared to mammography alone. The authors believe the technology's effectiveness could justify adding it to the screening routine for women with dense breasts or women at high risk for breast cancer. One important thing to take into account is that women with compressed breast thickness at mammography of greater than 7 cm were specifically not recruited because of ultrasound's limited effectiveness at these depths, according to the study team.[216]

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[209] Homepage of RadiologyInfo, *Image Gallery – Breast Ultrasound* [Online]
[210] Homepage of the Breast Center of Northwest Arkansas, *Ultrasound* [Online]
[211] Berg, W., Blume, J., Mendelson, E., Merritt, C., & Schleinitz, M., 2006, *Screening breast ultrasound in high-risk women*, American College of Radiology Imaging Network (ACRIN) [Online]
[212] Bruening, W., Kostinsky, H., Launders, J., Pinkney, N., Schoelles, K. & Turkelson, C., 2006, p. 84
[213] Homepage of New Choice Health – Medical Cost Comparison, *Breast Ultrasound Cost* [Online]
[214] The, W. & Wilson, A., 1998, pp. 449-50.
[215] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, pp. 133-134
[216] Ridley, E., 2009, *Automated whole-breast US doubles cancer detection* [Online]

Breast Physical Examination

Breast Physical Examination (BPE), also referred to as Clinical Breast Examination (CBE), is a manual examination of the breasts done by a doctor or other health care professional. The doctor seeks to detect breast abnormalities to find palpable breast cancers at an early stage of progression.[217]

The American Cancer Society (ACS) recommends that women in their 20s and 30s have a Breast Physical Examination every three years and after the age of 40 this exam should be done every year.[218] The method is not used as the only screening method but rather as a complement to mammography. The specificity of Breast Physical Examination is 94% and the sensitivity is 54%.[219] Studies have shown that the accuracy of BPE is highly dependent on time taken to do the examination.[220] Exact costs are not available but the method is likely to be inexpensive since no equipment is required.

About 20% of the breast tumors that are not seen on a mammogram are detected by a BPE.[221] A controversial Canadian study found that BPE is as effective as mammography in reducing mortality from breast cancer in women aged over 50. The scientists found that mammography detected breast cancers earlier than with BPE, but unexpectedly, earlier detection did not translate into a survival advantage.[222] The reliable of the study can be discussed; many other studies have shown that earlier detection of breast cancer is in fact leading to fewer deaths.[223]

A study published in the Journal of the National Cancer Institute (2009), shows that breast cancer rates and sensitivity was higher, but so were also the false-positive rates, among women who did a BPE in addition to Mammography. For a theoretical population of 10,000 women between ages of 50 and 69 years, the addition of BPE would lead to the detection of breast cancer in only four women

[217] Alciati, M., Baines, C., Barton, M., Bobo, J., Coleman, C., Dolan, M., Gaumer, G., Hannan, J., Kopans, D., Kutner, S., Lane, D., Lawson, H., Meissner, H., Moorman, C., Osuch, J., Pennypacker, H., Pierce, P., Saslow, D., Sciandra, E., Smith, R. & Coates, R., 2004, p. 327
[218] Burke, W., Costanza, M., Evans, P., Eyre, H., Foster, R., Hendrick, E., Saslow, D., Sawyer, K., Sener, S. & Smith, R., 2003, p. 143
[219] Alciati, M., McDonald, S. & Saslow, D., 2004, pp. 345-61.
[220] Knutson, D. & Steiner, E., 2007, p. 1660
[221] Homepage of Breastcancer.org, *Breast Physical Exam* [Online]
[222] Baines, C., Miller, A., To, T., & Wall, C., 2000, p. 1490
[223] Homepage of MedicineNet.com, *Cancer Detection & Treatment* [Online]

whose cancers would be missed by Mammography. However, adding BPE would also lead to false-positive results for an additional 219 women.[224]

Breast Self-Examination

In Breast Self-Examination (BSE) the women receive instructions by a health care professional so she can examine her own breast and hopefully detect any changes.[225] The American Cancer Society recommendations regarding BSE are that women in their 20s should be told about the benefits and limitations of the method. It is then up to the woman herself if she wants to implement them or not.[226]

The contribution of the Breast Self-Examination to early detection is difficult to determine. There is no available data on the method sensitivity or specificity, but the values can be assumed to be low. The methods cost is not available, but the method is inexpensive since no equipment is required and the only cost is associated with the woman's instructions.

In the recent years there have been a shift from formal teaching of a technique for Breast Self-Examination to only reinforcing the importance of a woman's being familiar with her breasts.[227] This change was implemented after findings from a large trial of Breast Self-Examinations conducted in Shanghai, China, showing that the practice of regular BSE by trained women does not reduce breast cancer-specific or all-cause mortality at all. In fact, there is as many cancers detected incidentally as were found by women trained to do routine Breast Self-Examinations. [228]

Another study, done by the Cochrane group, indicates that BSE increases the number of biopsies that is performed. The Cochrane group viewed this as evidence of harm and recommended that women should not perform Breast Self-Examination.[229]

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[224] Brown, P., Chiarelli, A., Mai, V., Majpruz, V., Shumak, R., Thériault, M., 2009, p. 1236
[225] American Cancer Society, 2007, p. 17
[226] Burke, W., Costanza, M., Evans, P., Eyre, H., Foster, R., Hendrick, E., Saslow, D., Sawyer, K., Sener, S. & Smith, R., 2003, p. 143
[227] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 49
[228] Allison, C., Chen, F., Gao, D., Ray, R., Thomas, D. & Wang, W., 2002, p. 1445
[229] Gøtzsche, P. & Kösters, J., 2009, *Regular self-examination or clinical examination for early detection of breast cancer* [Online]

Ductal Lavage

Ductal Lavage (DL) is a method where malignant cells can be found in fluid expressed from the breasts of women with breast cancer. The method was first suggested as a screening test in the 1950s by Dr. Papanicolaou, but the technique was developed first 2001 by Susan Love and her team.[230]

In Ductal Lavage a micro-catheter is inserted into the nipple and a small amount of salt water is released into the duct to rinse out cells. The fluid, then referred to as Nipple Aspirate Fluid (NAF), is pulled back out of the nipple and sent to the laboratory for analyze.[231]

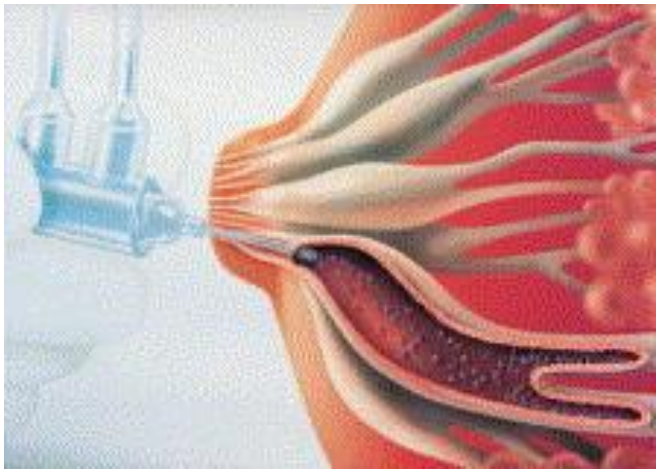

Figure 4.6 – The principle of **Ductal Lavage.**[232]

The American Cancer Society don´t recommend Ductal Lavage as an independent screening or even as a complement to mammography.[233] The specificity of Ductal Lavage is 96% and the sensitivity is 43%.[234] The cost is approximately $250 to $300 per procedure. [235]

[230] Anderson, B., Anderson, M., Arias, R., Cazzaniga, M., Clark, R., Dooley, W., Euhus, D., Elledge, R., Esserman, L., Ganz, P., Haffty, B., Hung, D., Kass, F., Kelley, M., Khan, S., King, B., King, E., Kuerer, H., Ljung, B., Love, S., O'Shaughnessy, J., Page, D., Phillips, R., Quiring, J., Schmit, P., Troyan S. & Veronesi, U., 2001, p. 1624
[231] Lindsey, H., 2001, p. 70
[232] Lindsey, H., 2001, p. 70
[233] Burke, W., Costanza, M., Evans, P., Eyre, H., Foster, R., Hendrick, E., Saslow, D., Sawyer, K., Sener, S. & Smith, R., 2003, p. 165
[234] Baird, C., Bethke, K., Bryk, M., Khan, S., Ljung, BM., Morro, M. Nayar, R., Rademaker, A., Ramakrishnan, R., Rodriguez, N., Staradub, V., Wiley, E. & Wolfman, J., 2004, p. 1510
[235] Lindsey, H., 2001, p. 70

By washing out a milk duct, the general area of the breast that has abnormal cells can be found, but not the exact location. So, Ductal Lavage must always be followed up with other tests.[236]

Ductal Lavage is meant to be used as a screening test for high risk groups, for example carriers of BRCA1/2 mutations. A recent study was conducted to evaluate the role of Ductal Lavage in breast cancer screening among these high-risk women. The results were that 74% of the potential candidates did not yield any NAF and 37% could not even have the duct cannulated. The women also found the technique painful and were reluctant to undergo multiple Ductal Lavage examinations over time. The researchers show this as evidence that Ductal Lavage is not likely to play any central role in breast cancer screening among high-risk women.[237]

Thermography

Thermography is a graphic display of the infrared radiation from the breast and has been used for breast cancer detection, as an adjunct to mammography, since 1982. Its inception dates to Lawson's observations in 1956 that breast cancer may be warmer than the surrounding tissue.[238] The method uses a special heat-sensitive imaging device to measure the temperature of the skin on the breast's surface. Because cancer cells are growing and multiplying very fast, blood flow and the metabolism are higher in a cancer tumor and therefore the skin temperature goes up.[239]

[236] Homepage of Breastcancer.org, *Ductal Lavage* [Online]
[237] Abati, A., Danforth, D., Filie, A., Giusti, R., Greene, M., Loud, J., Nichols, K., Prindiville, S. & Thiébaut, A., 2009, p. 1251
[238] Amalu, W., 2004, p. 1174
[239] Boné, B., 1997, p. 4

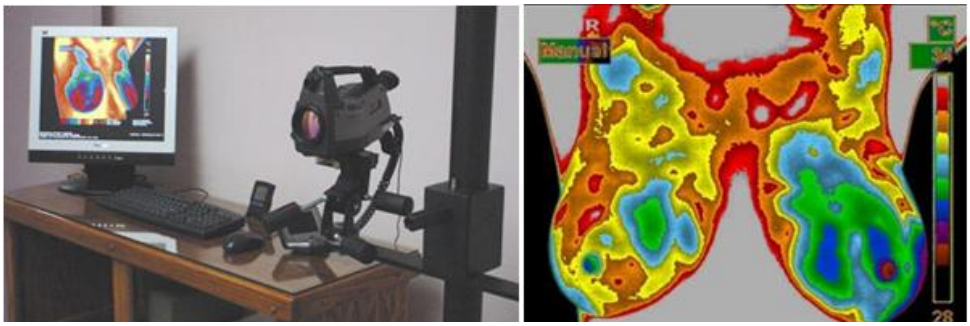

Figure 4.7 – The Thermography equipment and an infrared picture that shows a significant amount of heat in the right breast that indicates breast cancer.[240, 241]

The American Cancer Society does not recommend thermography as a replacement for mammography, but only as a supplement to help identify cancers that are close to the skin.[242] According to literature the sensitivity and the specificity are 85% and 70%, respectively.[243] The cost for a breast thermography examination is generally around $200, depending on radiologist reading fees.[244]

In April 2009 the Oregon Department of Justice shut down a health clinic in Medford because they had misrepresented the efficacy of thermography as a breast cancer detection tool. Ever since that there is an ongoing debate, with the major question: is thermography a legitimate adjunctive breast imaging technique or not? According to Dr. Leonard Berlin, chair of radiology at Rush North Shore Medical Center in Skokie, the problem is that the technique never has been proved clinically (or at least in no trustworthy study).[245]

[240] Homepage of Breastthermography.com, *What is the Procedure Like* [Online]
[241] Homepage of Breastthermography.com, *Case Studies* [Online]
[242] Homepage of Breastcancer.org, Thermography [Online]
[243] Francis, J., Haberman, J. & Love, T., 1980, p. 492
[244] Homepage of Therma Screen, *Thermography* [Online]
[245] Yee, K., 2009, *Oregon case spotlights clinical validity of breast thermography* [Online]

4.2.2 Diagnostic Tests

Biopsy

A biopsy is a small operation done to remove tissue from an area of concern in the body, either by a very thin needle, *fine-needle aspiration* (FNA) or with a larger needle, so called *coarse-needle biopsy* (CNB).[246] The tissue sample is then examined by a pathologist to establish whether the lump is malignant or benign.[247] Biopsy is the most common method to classify the tumor, but it is not an imaging test that can determine location or size of the tumor.

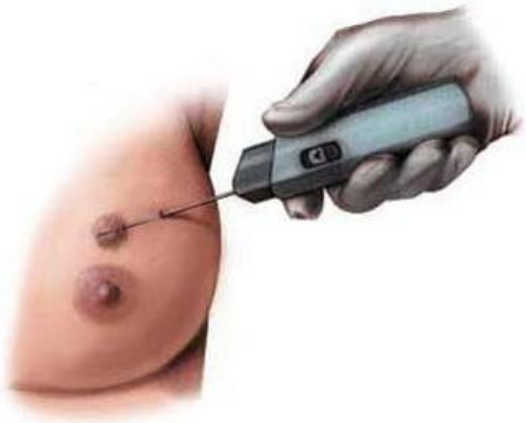

Figure 4.8 – The procedure of a coarse-needle biopsy.[248]

Biopsy has 100% specificity and the sensitivity is 82% for CNB and 75% for FNA.[249] The cost of CNB and FNA is approximately $400 and $250, respectively.[250]

In the United States, 20% of women who have biopsies turn out to have cancer. In Sweden where only the most suspicious cases are biopsied, 80% of the biopsies turn out to be cancerous.[251]

A major study performed by Bruening et al. (2006) evaluated biopsy compared to non-invasive diagnostic tests. The researchers concluded that none of the non-

[246] Homepage of Emory University, *Cancer Diagnosis: Core Needle Biopsy (CNB)* [Online]
[247] Homepage of Breastcancer.org, *Biopsy* [Online]
[248] Homepage of UC Davis Health System, *Biopsy figure* [Online]
[249] Andrews, V., Lilley, L., Radford, L., Rao, R. & Ulissey, M., 2009, p. 1170
[250] Andrews, V., Lilley, L., Radford, L., Rao, R. & Ulissey, M., 2009, p. 1170
[251] Homepage of Breastcancer.org, *Biopsy* [Online]

invasive diagnostic tests (MRI, Sonography, PET and Nuclear Medicine Breast Imaging) were accurate enough to replace biopsy.[252]

Magnetic Resonance Imaging

MRI can classify if tumors are malignant or benign. The visualization is based on rapid enhancement after the administration of the contrast agent as well as morphologic characteristics. Malignant tumors, including DCIS, tubular carcinoma and invasive lobular carcinoma, have slower, less intense enhancement patterns than benign tumors.[253] There is also computer-aided kinetic information that further enhancing the methods ability to distinguish malignant from benign tumors.[254] However, MRI is also associated with false positives. In one study of 48 patients, MRI overestimated the extent of disease in 21%.[255]

Studies have shown that MRI can demonstrate the extent of cancer in the breast more accurate than Mammography, Sonography and Positron Emission Tomography.[256]

The MRI method can also be used to see if the cancer has traveled outside the breast, for example whether there are any cancer cells in the lymph nodes. Whether or not there are cancer cells in the lymph nodes is an important factor doctors consider when deciding if chemotherapy or radiation therapy should be given after surgery to lower the risk of the cancer coming back. Today, the nodes are examined during surgery.[257]

Tumor Marker Tests

In a Tumor Marker test the doctor takes a sample of blood, urine or body tissue and sends it to a laboratory to look for, so called, *tumor markers*. Tumor markers are substances, usually proteins, which are produced by cancer cells or by other

[252] Bruening, W., Kostinsky, H., Launders, J., Pinkney, N., Schoelles, K. & Turkelson, C., 2006, pp. 96-98
[253] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 112
[254] DeMartini, W., Lehman, C., Partridge, S., Peacock, P. & Wang, L., 2009, p. 826
[255] Allison, K., De Paredes, E. & Smith, M., 2006, p. 318
[256] Orel, S. & Schnall M., 2001, p. 23
[257] Bittner, N., DeMartini, W., Eby, P., Kim, J., Lehman, C., Loiselle, C., & Peacock, S., 2008, p. S176

cells of the body in response to cancer. Tumor markers are also called *serum markers* or *biomarkers*.[258] Examples of tumor markers are: CA 15.3, CA 549, CEA and MCA.

The sensitivity of the method differs depending on the tumor marker that are sought, for example are the sensitivity for CEA 45%, for MCA 59%, for CA 15.3 71% and for CA 549 72%.[259] There are no available data about the specificities of the methods. According to literature are the tests very expensive, but there are no available data of exact costs.[260]

Oncologists use tumor marker tests to diagnose and monitor cancer. These tests can be used to determine whether or not cancer is present, i.e. if the tumor is malignant or benign and to help determine the stage of the cancer. Tumor marker tests are also used to measure the progress during treatment. If the tumor marker levels decrease, then the cancer is responding to the therapy, an increased level indicates that the cancer is resisting the treatment. These tests are not imaging tests so they can't determine size or location of the tumors.[261]

Mammography

Mammography has an established role in breast cancer diagnosis. It is used to define the extent of malignancy before surgery and to monitor the breast after surgery and radiation therapy.[262] Mammography is also used to guide biopsies.[263]

Diagnostic mammograms are different from screening mammograms in that they focus on getting more information about a specific area of concern, usually due to a suspicious screening mammogram. In diagnostic mammography more pictures are taken than in a screening mammogram.[264]

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[258] Homepage of American Society of Clinical Oncology (ASCO), *Understanding Tumor Markers* [Online]
[259] Martoni, A., Zamagni, C., Bellanova, B., Cacciari, N., Martoni, A., Pannuti, F., Strocchi E., Vecchi, F., Zamagni, C., & Zanichelli, L., 1995, p. 1615
[260] Homepage of Breastcancer.org, *Blood Marker Tests* [Online]
[261] Homepage of About.com, *Tumor Marker Test Overview – Breast Cancer Tumor Marker Tests* [Online]
[262] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 84
[263] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 84
[264] Homepage of Breastcancer.org, *Mammograms* [Online]

Sonography

Sonography is one of the most frequently used diagnosis tools to classify abnormalities of the breast. With sonography it is possible to determine the location, size, shape and to see whether a breast lump is fluid-filled (a cyst) or if it is a solid lump. [265] A lump that has no fluid or that has fluid with floating particles may need more tests.[266]

One advantage of the method is that images can be obtained from almost any orientation.[267] Because Sonography provides real-time images, it is also often used to guide biopsy procedures.[268]

Sonography can´t show areas deep inside the breast or show micro calcifications.[269] Sonography cannot always determine whether a solid lump is cancerous, nor can it detect DCIS, because the volume of the intraductal lesion is usually too small.[270, 271]

Nuclear Medicine Breast Imaging

The Nuclear Medicine Breast Imaging starts with an injection of a radioactive tracer. The local concentration of radioactive tracer is higher for cancer cells than for normal cells. Imaging can begin 5 to 15 minutes after the administration of radiotracer.[272] The patient are then lying face down on a special table while the breast hangs down through an opening in the table. A special gamma camera is then used to take images of the breasts. The method involves the use of radiation.[273]

The method is not only referred to Nuclear Medicine Breast Imaging, sometimes it is called Molecular Breast Imaging or Scintimammography. Currently, only the

[265] Homepage of RadiologyInfo, Breast Ultrasound [Online]
[266] Homepage of WebMD, Breast Ultrasound [Online]
[267] Homepage of About.com, *Breast Ultrasound - Imaging for Breast Abnormalities* [Online]
[268] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 122
[269] Homepage of About.com, *Breast Ultrasound - Imaging for Breast Abnormalities* [Online]
[270] Homepage of Breastcancer.org, *Ultrasound* [Online]
[271] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 125
[272] Ingui, C., Karstaedt, P., Nguyen, B., Ram, P. & Roarke, M., 2009, p. 71
[273] Imaginis Report, 2001, *Nuclear Medicine Breast Cancer Test May Be Helpful for Some Women, Particularly in Those with Dense Breasts*, Imaginis Report, September issue, [online]

Miraluma Tc-99m sestamibi compound, manufactured by DuPont Pharmaceuticals, is approved for breast imaging. Therefore, the Nuclear Medicine Breast Imaging test may also be referred to as a "Miraluma test".[274]

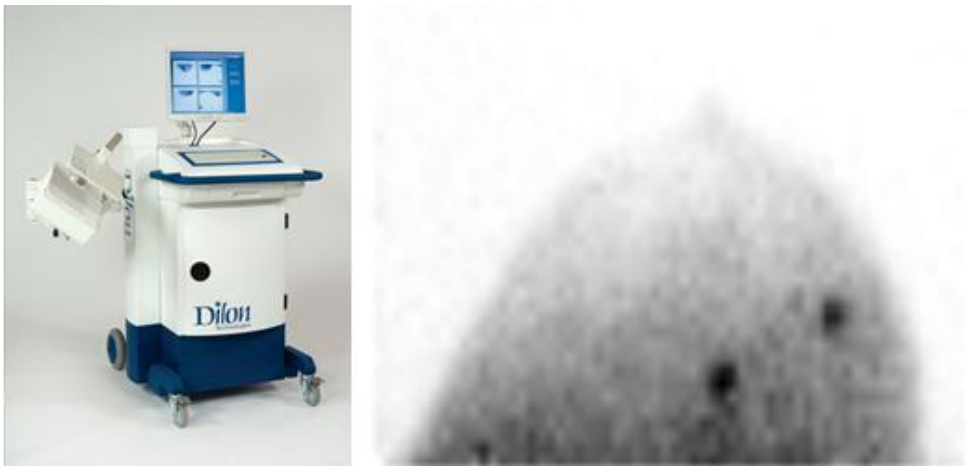

Figure 4.9 – The Nuclear Medicine Breast Imaging equipment and a picture taken with the technology.[275]

Nuclear Medicine Breast Imaging has 84.8% specificity and 68.7% sensitivity.[276] The test takes approximately 45 minutes to one hour to perform and costs $200 to $600 per exam.[277]

Nuclear Medicine Breast Imaging is used to determine the size and the location of the tumor and to help physicians classifying the tumor, based on the accumulation of the radiotracer.[278] Studies show that nuclear medicine breast imaging are 90% accurate in detecting abnormalities over one centimeter, but only 40% to 60% accurate in imaging small breast abnormalities (less than 1cm) and are unable to identify DCIS.[279, 280]

[274] Homepage of Imaginis, *Nuclear Medicine Breast Imaging (Scintimammography)* [Online]
[275] Homepage of Radiological Society of North America (RSNA), *New Breast Imaging Technology Targets Hard-to-Detect Cancers* [Online]
[276] Bruening, W., Kostinsky, H., Launders, J., Pinkney, N., Schoelles, K. & Turkelson, C., 2006, p. 35
[277] Homepage of Imaginis, *Nuclear Medicine Breast Imaging (Scintimammography)* [Online]
[278] Bombardieri, E., Bonadonna, G. & Gianni, L., (eds.), 2008, p. 58
[279] Homepage of Imaginis, *Nuclear Medicine Breast Imaging (Scintimammography*) [Online]
[280] Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), 2008, p. 114

Nuclear Medicine Breast Imaging has no limitation regarding dense breasts or the presence of scar tissue or implants.[281]

In an Italian study, mammography and Nuclear Medicine Breast Imaging were compared. While the overall accuracy of the two tests were similar, Nuclear Medicine Breast Imaging was better to see the breast cancer in younger women.[282]

Computerized Tomography

The first reports of computerized tomography (CT) for evaluating breast disease was described 1977 by Chang. A CT scan is an X-ray technique that gives information about the body's internal organs in 2-dimensional slices. During a CT scan, the patient lies on a table that passes through a doughnut-shaped machine. A computer puts the x-rays together to create detailed pictures of the inside of the body. Before the test, a contrast agent is injected.[283]

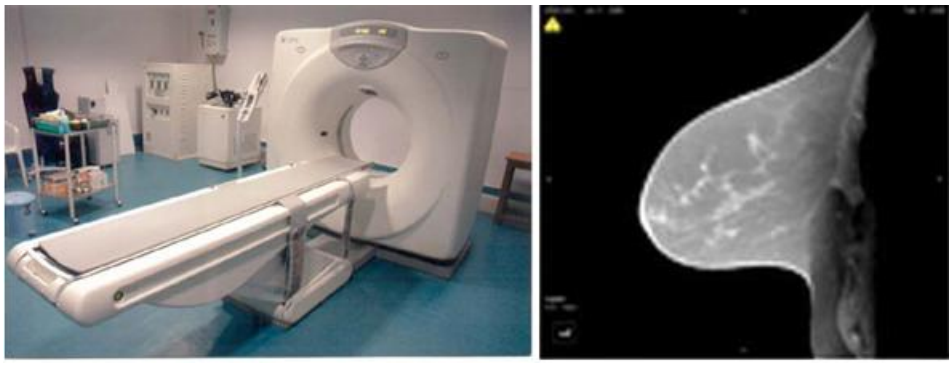

Figure 4.10 – A CT scan and a CT image of a breast. [284,285]

The sensitivity and the specificity are at mediocre level, 71.9% and 83.3%.[286] The cost of a CT scan is between $500 and $700.[287]

[281] Bombardieri, E., Bonadonna, G. & Gianni, L., (eds.), 2008, p .68
[282] Brandes, A., Bui, F., Feretti, G., Geatti, O., Lumachi, F., Marzola, C., Povolato, M. & Zucchetta, P., 2001, p. 2201
[283] Boné, B., 1997, p. 3
[284] Homepage of World Culture Pictorial, *CT figure* [Online]
[285] Homepage of Top News, *CT figure* [Online]

The method is often used to assess whether or not the cancer has moved into the chest wall. This helps determine whether or not the cancer can be removed with mastectomy. The method is also used in order to examine other parts of the body where breast cancer can spread, such as the lymph nodes, lungs, liver, brain and spine. It also used to see whether or not the cancer is responding to the cancer treatment.[288]

The CT provides three-dimensional images of the breast, compared with just two-dimensional images for mammography, which eliminates image artifacts (suspicious areas that result from normal breast structures overlaying each other when the breast compresses).[289]

The radiation dose received during a breast CT is about the same amount of radiation a person gets from the natural surroundings in an average 2-years period (7 mSv).[290] This greatly exceeds the American College of Radiology recommendation of ≤ 3 mSv. Breasts CT can therefore actually lead to cancer, but the potential carcinogenic effects are unknown.[291]

Because of the high cost of the examination and the high radiation dose is an inappropriate breast cancer screening tool and is only used in selected cases to show the extension of metastasis and to reveal skeletal destruction of the sternum and chest wall.[292]

Positron Emission Tomography

Positron Emission Tomography (PET) for breast was first described in 1988 by Mintun.[293] The method can detect areas of cancer by obtaining images of the body's cells as they work. Before a PET scan, a small amount of radioactive

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[286] Akiyama, F., Furusawa, H., Hideyuki Wakamatsu, H., Ifuku, H., Matsu, T., Nakahara, H., Nakahara, M. Namba, K., Shirouzu, M., Tamura, S., Tanaka, C. & Watanabe, R., 2002, p. 17
[287] The BFP Project Biomonitoring Futures, 2006, p. 6
[288] Homepage of Breastcancer.org, *CT (CAT) Scans* [Online]
[289] Homepage of National Institute of Biomedical Imaging and Bioengineering (NBIB), *Dedicated Breast CT Scanner Offers Alternative to Mammography* [Online]
[290] Homepage of RadiologyInfo, *Safety* [Online]
[291] Camacho, M., Hui, F. & Parker, M., 2005, p. 1228
[292] Boné, B., 1997, p. 3
[293] Brodack, J., Katzenellenbogen, J., Mathias, C., McGuire, A., Mintun, M., Siegel, B. & Welch, M., 1988, p. 45

material is injected into the bloodstream and because cancer cells tend to be more active than normal cells, they also absorb more of the radioactive material. A special camera then scans the body to pick up any highlighted areas on a computer screen. [294]

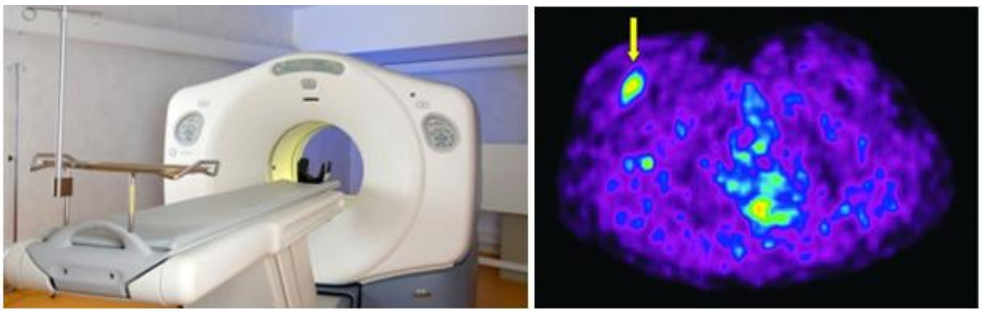

Figure 4.11 – The PET scan equipment and an image taken with PET. The yellow arrow indicates a primary tumor.[295]

The sensitivity and specificity of PET in detecting malignant breast lesions is 93% and 75%, respectively.[296] The cost of a PET examination is around $5,000 per scan.[297]

PET can be used for detecting and staging breast cancer.[298] PET scans can also help the doctor evaluate whether cancer still exists after radiation or chemotherapy and to see if the cancer has spread to the lymph nodes or other parts of the body.[299]

PET has low sensitivity for small lesions and for slow-growing tumors such as DCIS and lobular carcinoma. [300] A PET scan gives radiation equivalent with six months of background radiation.[301]

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[294] Homepage of Breastcancer.org, *Whole-Body PET Scans Have High False Positive Rates for Breast Cancer* [Online]
[295] Homepage of Läkartidningen, *PET figur* [Online]
[296] Buck, A., Glatting, G., Guhlmann, A., Hörster, T., Koretz, K., Kreienberg, R., Kühn, T., Nüssle, K., Reske, S., Rieber, A., Santjohanser, C. & Schirrmeister, H., 2001, p. 351
[297] Homepage of Breastcancer.org, *Whole-Body PET Scans Have High False Positive Rates for Breast Cancer* [Online]
[298] Benard, F. & Turcotte, E., 2005, p. 158
[299] Homepage of Breastcancer.org, *Whole-Body PET Scans Have High False Positive Rates for Breast Cancer* [Online]
[300] Ingui, C., Karstaedt, P., Nguyen, B., Ram, P. & Roarke, M., 2009, p. 80
[301] Bruening, W., Kostinsky, H., Launders, J., Pinkney, N., Schoelles, K. & Turkelson, C., 2006, p. 34

4.2.3 Summary of the Techniques for Breast Cancer Detection

In Table 4.4 and 4.5 the different methods for detection of breast cancer are being compared based on the sensitivity, specificity and cost. The symbol "-" means that no information could be found.

Screening tests			
	Sensitivity [%]	Specificity [%]	Cost [$]
Mammography	79	95.7	150-200
Magnetic Resonance Imaging (MRI)	92.5	72.4	1,000-1,500
Sonography	86.1	66.4	150
Breast Physical Examination	54	94	-
Breast Self-Examination	-	-	-
Ductal Lavage	43	96	250-300
Thermography	85	70	200

Table 4.4 – Summary of the screening tests.

Diagnostic tests			
	Sensitivity [%]	Specificity [%]	Cost [$]
Biopsy	FNA 75 CNB 82	100	FNA 250 CNB 400
Magnetic Resonance Imaging (MRI)	92.5	72.4	1,000-1,500
Tumor Marker Tests	CEA 45 MCA 59 CA 15.3 71 CA 549 72	-	-
Mammography	79	95.7	150-200
Sonography	86.1	66.4	150
Nuclear Medicine Breast Imaging	68.7	84.8	-
Computerized Tomography	71.9	83.3	500-700
Positron Emission Tomography	93	75	1,000-1,500

Table 4.5 – Summary of the diagnostic tests.

5. Analysis of the MRI Technology

Chapter five contains an analysis of the current MRI technology. The advantages and disadvantages, as well as possible areas for improvement, of the technology are discussed.

5.1 MRI as a Screening Test

Suitability criteria for a screening test include adequate sensitivity and specificity, low cost, easy administration, high safety and to impose minimal discomfort for the patients.

The general method used today to screen for breast cancer is mammography, probably because of its low cost, high specificity and reasonable sensitivity. All other screening tests mentioned earlier are in fact not used on their own as a screening tool, rather as complements to mammography.

The mammography is however not perfect. As previously mentioned, mammography involves ionizing radiation that can produce adverse health effects. MRI, on the other hand, uses radio-frequency waves, which are photons with energy levels lower than visible light. This low-energy radiation is non-ionizing and is considered much safer than ionizing radiation.[302]

Hundreds of women who participate in mammography screening programs are falsely reassured that they are free from breast cancer each year.[303] MRI is significantly more sensitive in detecting cancers than mammography; 92.5% compared to 79%.[304] The sooner cancer is diagnosed and treated, the better are the chances of full recovery, so if MRI was used as a screening tool there is no doubt that more lives could be saved.

Mammography has also been the mainstay for the detection and evaluation of Ductal Carcinoma In Situ.[305] However, MRI has gained increased popularity in the evaluation of DCIS after it had been shown that MRI is in fact better than mammography at finding DCIS. Since MRI appears to be better than

[302] Masha, Z., 2002, p. 3
[303] Liberman, L. & Morris, E., 2005, p. ix
[304] Bruening, W., Kostinsky, H., Launders, J., Pinkney, N., Schoelles, K. & Turkelson, C., 2006, p. 67
[305] Allison, K., De Paredes, E. & Smith, M., 2006, p. 308

mammograms at detecting DCIS, more women who get screening MRIs will be diagnosed and treated for DCIS. This will reduce their risk of invasive breast cancer in the future. However, even though the sensitivity of MRI in detecting DCIS is shown to be higher than for mammography, the specificity was also lower.[306]

Mammograms can be difficult to conduct in younger women because their breast tissue is dense. Therefore, Sonography is used to screen these younger women.[307] MRI has, however, a higher sensitivity and specificity and will probably take over this roll in the future. MRI is also superior to mammography in detecting cancer in patients with breast implants and cancers in the contralateral breasts of women diagnosed with breast cancer.[308]

Although magnetic resonance imaging shows promise as a screening tool, it is not currently recommended for general screening because of high false-positive rates (the specificity is only 72.4% compared to 95.7% for mammography) and high cost (1,000 to $1,500 per scan compared to $150 to $200 for a mammography). The cost is, however, something that can be discussed; it is not certain that the total cost will increase, as more patients receive their diagnosis earlier, which means less expensive treatments and higher survival rates. However, the low specificity means unnecessary recalls and biopsies, which also add to the total cost.

We are likely to observe a paradigm shift in the manner in which breast cancer screening will be performed in the future. Breast cancer screening is currently performed in a standard manner for all women with mammography. However, this level of standardization is likely to be replaced by tailored screening programs with respect to the women's individual risk of developing breast cancer. More and better tools are also being developed to find these women with increased risk for breast cancer, see Appendix C. Already elements of this change can be observed with the recommendation by American Cancer Society to use MRI for screening of these high-risk women. It is also this segment, screening high risk patients, which is the most important market segment for MRI in the field of breast cancer.

[306] Birdwell, R., Daniel, B. & Ikeda, D., 2000, p. 50
[307] The, W. & Wilson, A., 1998, pp. 449-50.
[308] Aspelin, P., Boné, B., Isberg, B., Perbeck, L. & Veress, B., 1995, p. 111

It is important to mention that the various screening tests do not always compete with each other, sometimes they actually complementing each other. Because mammography has a low sensitivity, about 10% of the women who had a mammogram will require more screening tests.[309] It is therefore interesting to compare MRI, not only with mammography, but also with other screening methods.

Both Breast Physical Examinations and Ductal Lavage are cheap, have a high specificity and don´t involve any radiation. The two methods have, however, really low sensitivities, so if tumors were not found with mammography they probably not will be found with the BPE or DL either.

Thermography has reasonable sensitivity and specificity but the method can't detect cancers that are deeper in the breast or small cancers that don´t generate any heat. So the usefulness of this method is limited and the technique will probably not be commercially used to detect breast cancer.

The MRI method´s major advantage compared to other screening tests is the high sensitivity, but the drawback is the relatively low specificity, which results in more recalls and biopsies.

[309] Homepage of Breastcancer.org, *Mammography: Benefits, Risks, What You Need to Know* [Online]

5.2 MRI as a Diagnostic Test

Diagnostic tests are used to classifying the tumors and to gather more information about the cancer, for example tumor size and exact localization, to guide decisions about treatment.

For the purpose of classifying the tumor, i.e. to determine if the tumor is malignant or benign, biopsy is undoubtedly the most common method used today. However, only a low percentage of women undergoing biopsy actually have cancer, meaning unnecessary operations for the patients. Therefore, there is a demand for non-invasive diagnostic tests that are as accurate as biopsy. A major study performed by Bruening et al. (2006) evaluated the non-invasive diagnostic tests (MRI, Sonography, PET and Nuclear Medicine Breast Imaging) to see if there are any substitutes to biopsy. Their result was that none of the diagnostic tests, not even MRI, were accurate enough to replace biopsy.[310]

Various imaging techniques (MRI, mammography, Nuclear Medicine Breast Imaging, CT, Sonography and PET) are used to determine the size and localization of the tumors. The most common methods are probably mammography and sonography. However, the high soft tissue contrast and three-dimensional format of MRI allows anatomic structures of the breast to be viewed in great detail. MRI can therefore demonstrate the extent of cancer in the breast more accurate than all other imaging tests (inclusive mammography and sonography).[311]

The MRI method can also be used to see if the cancer has traveled outside the breast and to see if there are any cancer cells in the lymph nodes. Today, the nodes are examined during surgery, but as the study shows, MRI could be a better alternative.[312]

Once breast cancer is diagnosed, many tests are used during and after treatment to monitor how well therapies are working. Monitoring tests also may be used to check for any signs of recurrence. Today, most follow-ups are made with mammography, despite that numerous studies have shown that MRI is superior to

[310] Bruening, W., Kostinsky, H., Launders, J., Pinkney, N., Schoelles, K. & Turkelson, C., 2006, pp. 96-98
[311] Orel, S. & Schnall M., 2001, p. 23
[312] Bittner, N., DeMartini, W., Eby, P., Kim, J., Lehman, C., Loiselle, C., & Peacock, S., 2008, p. S176

mammography (and Sonography) for estimating tumor size. Tumor size is one of the most important factors when monitoring the progress of the therapy.[313]

Why the MRI technique isn't used to a higher extent for diagnostic purposes (determine size and localization of tumors) probably depends on a combination of a lack of availability, limited expertise of radiologists and the risk of overestimating the extent of disease.

5.3 Summary of MRI´s Strength and Weaknesses

To understand the characteristics of the MRI technology in a clear way, the most important strengths and weaknesses of the method is summarized in the text below.

The strength of the MRI technology is the high sensitivity (92.5%). MRI also uses radio-frequency waves, which is non-ionizing energy and considered safe. MRI has no limitations in terms of detecting cancer in dense breasts or in breasts with implants.

The major weakness of the MRI technology is the low specificity (72.4 %), meaning that many patients will be misdiagnosed. The cost is also relatively high, $1,000 to $1,500 per scan.

[313] Hylton, N, 2005, pp. 1679-1680

6. Empirics and Analysis of SPAGO´s Contrast Agent

Chapter six contains a description of SPAGO´s contrast agent and a brief overview of the market of MRI and the existing contrast agents. The chapter also includes a SWOT analysis of SPAGO´s product.

6.1 Empirics: Product Description

SPAGO´s contrast agent is based on the so-called SPAGO-Platform: Safe Paramagnetic Gadolinium Oxide nanoparticles. The nanoparticles consist of gadolinium ions (Gd^{3+}), which is a metal ion with special magnetic properties that allows it to enhance the tissue contrast in MRI. There are 1000-2000 gadolinium ions in every particle (conventional contrast agents have only one) and the ions have a higher individual efficacy than in conventional contrast agents. The size of a particle is approximately 10 nm in diameter and therefore small enough for being entirely excreted through the kidneys after administration.[314]

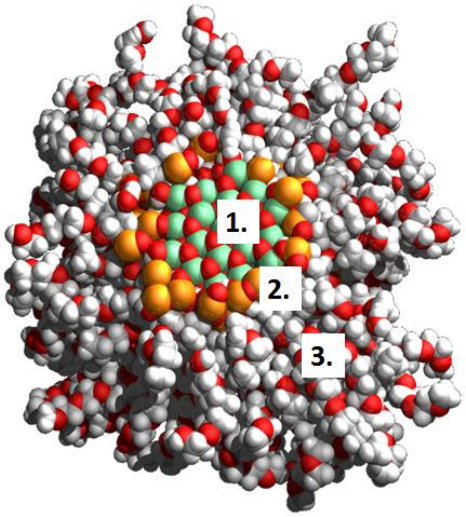


Figure 6.1 – A particle of SPAGO´s contrast agent.[315]

The gadolinium core (1) is encapsulated by a silicate network (2) and the surface is coated with a bioinert and durable polyether shell (3), see Figure 6.1. The shell encapsulates and protects the gadolinium ions from degradation.

[314] Axelsson, O., personal communication, September 8, 2009
[315] Axelsson, O. (oskar.axelsson@spagoimaging.se), 12 August, 2009 [e-mail]

In the future, the idea is that the shell also will serve as attachment points for targeting molecules, which are molecules targeting a unique chemical structure of the diseased cell. This kind of imaging is called *molecular imaging* and is not possible today in MRI due to far too weak signal enhancement of the conventional MRI contrast agents. The contrast of the particles in SPAGO´s contrast agent is however higher, enough to enable molecular imaging in MRI, hence improving selective localization of diseased cells.[316]

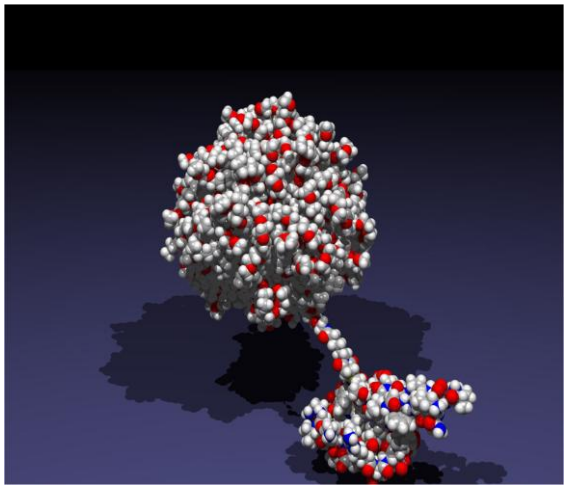


Figure 6.2 – A SPAGO particle with a fixed target molecule.[317]

SPAGO´s contrast agent can selectively penetrate into tumor tissue, thus achieving what is called *passive tumor targeting*. Tumors have lots of small blood vessels around them. The walls in these blood vessels are composed of endothelial cells, which are usually damaged. Instead of being tightly packed blocks (as for healthy blood vessels) they are more irregular in structure, creating holes in the blood vessel walls. Since SPAGO's product consists of thousands of ions the particles are so large that they do not penetrate healthy vessels (or in to inflammatory tissue), which the commercial contrast agents do. However, the contrast agent can get through the holes formed in the damaged blood vessels. SPAGO´s contrast agent will therefore only distribute in approximately 5 liters, while the contrast agents that is available on the market today is spreading evenly all over the body and has a distribution volume of 50 liters.[318]

[316] Axelsson, O., personal communication, September 8, 2009
[317] Axelsson, O. (oskar.axelsson@spagoimaging.se), 12 August, 2009 [e-mail]
[318] Axelsson, O., personal communication, October 14, 2009

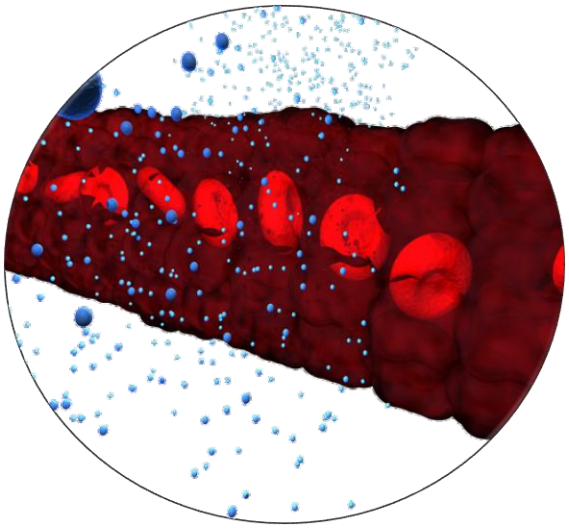


Figure 6.3 – Passive tumor targeting.[319]

The contrast agent is injected intravenously and the MRI study is performed after one to two hours.[320]

One important thing regarding gadolinium-based contrast agent is that the U.S. Food and Drug Administration (FDA) and other medical agencies recently have recognized some safety issues in connection with the use of conventional non-encapsulated gadolinium-based contrast agents (GBCA). [321]

Nephrogenic Systemic Fibrosis (NSF), also known as Nephrogenic Fibrosing Dermopathy (NFD), is a sometimes fatal condition that can cause fibrosis of the bone, kidneys, lungs, muscle and other structures. Although the cause of the disease is not fully understood, it has been closely connected to patients with kidney problems who receive large doses of GBCA.[322] A survey shows that approximately 400 cases of NSF have been reported worldwide and as many as 90% of them had previously received gadolinium-based contrast agents.[323] U.S. Food and Drug Administration (FDA) are now investigating the relationship

[319] Axelsson, O. (oskar.axelsson@spagoimaging.se), 12 August, 2009 [e-mail]
[320] Axelsson, O., personal communication, October 14, 2009
[321] Homepage of The International Center for Nephrogenic Fibrosing Dermopathy Research (ICNFDR), *NSF – what is it?* [Online]
[322] Homepage of The International Center for Nephrogenic Fibrosing Dermopathy Research (ICNFDR), *NSF – what is it?* [Online]
[323] Abu-Alfa, A., Cowper, S., Kanal, E. & Kuo, P., 2007, p. 647

between NSF and gadolinium. In the meantime, the FDA advises cautionary use of all gadolinium-based contrast agents in patients with renal disease.[324]

6.2 Empirics: Market Description

The overall market for MRI equipment is steadily increasing and is expected to reach $3.5 billion by 2012 according to a report by the market research firm InMedica, a division of IMS Research of Wellingborough, U.K.[325] The United States is the largest market among the world's nations and between the year 2000 and 2005 the number of MRI scanners in the U.S. more than tripled, from 7.6 to 26.6 machines per million people.[326] Other major markets are Western Europe and Japan.[327] Growing MRI markets are also found in less developed nations in Asia, Latin America and Eastern Europe.[328]

The number of MRI procedures is also predicted to increase, which strongly indicate a growing market for the MRI-contrast agents. Table 6.1 shows the predicted imaging procedures in the United States 2007-2009.

	Procedures [millions]		
Modality	**2007**	**2008**	**2009**
Ultrasound	90.6	101.8	115.1
SPECT	28.8	32.2	36.3
MRI	34.1	36.9	39.7
CT	77.6	87.3	98.6
PET	1.8	2.1	2.4

Table 6.1 – Number of U.S. imaging procedures by modality 2007-2009.[329]

MRI to screen for breast cancer have also been increasing in recent years and at the same time, mammography screening has been decreasing. Nearly 25 % of all breast cancer screenings in the United States were done by MRI in 2006, almost double the number compared to 2003.[330]

An important thing to mention in this context is the 2004 European Commission (EC) directive regarding applied electromagnetic fields. This directive

[324] Homepage of Doctors Guide, *MRI Contrast Agent Linked to Rare Disease* [Online]
[325] Homepage of AuntMinnie.com, *Refurbished MRI biggest competition to new systems* [Online]
[326] Baker, L. & Baras, J., 2009, p. w1133
[327] Masha, Z., 2002, p. xxii
[328] Freedonia Group, 2004, p. 1
[329] Smith, J., 2005, p. 51
[330] Homepage of Breastcancer.org, New scans prompt mastectomies for breast patients [Online]

(2004/40/CE) gives upper limits on applied electromagnetic fields and could potentially have a severe impact on the MRI technology. Investigations conducted by the EC and the U.K. government concluded that MRI workers routinely exceed the exposure limits in the directive, however they didn't experiences any ill effects as a result. This fact led the EC to postpone the directive until April 2012.[331] In the EU legal system, directives are binding and must be transposed into national legislation by all member states.[332]

6.3 SWOT Analysis of SPAGO´s Contrast Agent

6.3.1 Internal Analysis: Strengths and Weaknesses

The management of SPAGO Imaging AB has to be aware of the advantages and disadvantages of their new MRI contrast agent. The overall evaluation of their product is therefore presented in form of a SWOT analysis.

The internal capabilities of the product of SPAGO Imaging AB are identified and analyzed. The strengths are internal factors, which can be seen as the *competitive advantages* and the weaknesses can, in the same way, be seen as *competitive disadvantages*. Important to note is that the product is in a development phase where the precise data is not completed. The product will, however, not be released to the next phase of development until the strengths that are listed below have been achieved.

Strengths:

- Higher contrast

Not only are there more than thousand of Gadolinium ions in every SPAGO particle, where conventional contrast agents have only one, but they also have a higher individual efficacy. Hence, SPAGO´s contrast agent gives a higher contrast than the conventional contrast agents. This is also leading to a possibility to find tumors earlier, when they still is very small. Identifying the tumors early improve the probability of a successful treatment.

[331] Le Bihan, D., 2009, Threats to ultrahigh-field MRI in Europe [Online]
[332] Herbillon, G., 2007, Introduction to the EC Directive 2004/40/CE – Obligations of employers (risk assessment, protective measures, worker information and training) [Online]

- Selective accumulation in diseased tissue

One attractive possibility to improve cancer diagnosis is to utilize the optimal size of SPACO´s contrast agent to selectively penetrate into tumor tissue, achieving *passive tumor targeting*. This leads to sharper boundaries of the tumor which can improve cancer detection and surgery planning.

- High specificity

SPAGO´s contrast agent don´t penetrate in to inflammatory tissue, this lead to better distinguish between cancerous- and inflammatory tissue. That, together with the better contrast and clearer boundaries, strongly indicates that the specificity will increase. It will be easier to see if there actually is a tumor or not.

- Lower dose of contrast agent

Because SPAGO´s contrast agent only will distribute in approximately 5 liters, compared to the commercial contrast agents that has a distribution volume of 50 liters, the administration dose will be much lower. Lower doses are always desirable because of cost and safety reasons.

- Safe

Another property of SPAGO´s contrast agent is the safe design. A bioinert and durable shell encapsulates and protects the Gadolinium ions from degradation. This means that the particles are expected to interfere minimally with normal cells and tissues. Furthermore, the size of the intact particle is small enough for being entirely excreted through the kidneys out in the urine.

- Enables Molecular Imaging for cancer diagnostics

SPAGO´s product is a promising candidate for molecular imaging, but this requires development of a new product, meaning new clinical trials.

Weaknesses:

- Small tumors with no vascular tissue

Small tumors have sometimes not had time to get vascular tissue. The principle of selectively penetration into diseased tissue would therefore not work. The contrast agent will however still has the basic function as a contrast agent.

- One-hour waiting period

It takes up to two hour after the contrast agent has been injected before the pictures can be taken. The waiting time is not only disturbing for the patient but it can cause organizational problems.

- New player

Another weakness that is connected to the company of SPAGO Imaging AB is that they are a new player on the market ant therefore not known within this field.

6.3.2 External Analysis: Opportunities and Threats

This section is based upon data from the analysis of the market environment. The opportunities and threats that the product of SPAGO Imaging AB faces from outside influences are listed.

Opportunities:

- Growing MRI market

The MRI market in the field of breast cancer is increasing. It may be that more doctors and women want the most sensitive test to find early-stage breast cancer, even if it means more false positives. Or it could be due to the American Cancer Society´s new recommendations to use MRI screening in high-risk women. New tools to identify high-risk groups are also being developed (see Appendix C) and that will most truly lead to an even greater use of the MRI equipment.

Since the market of the MRI contrast agents is strongly linked to the MRI market will a growing MRI market lead to a more frequent use of MRI-contrast agents which is a great opportunity to SPAGO Imaging AB.

- Safety issues in non-encapsulated Gd-based contrast agents

The concern about Nephrogenic Systemic Fibrosis only involve non-encapsulated Gd-based contrast agent. Because the SPAGO´s contrast have a bioinert shell that encapsulates the Gadolinium ions from degradation can SPAGO´s product actually benefit from this discovery.

Threats:

- New product introduction

There is always a risk in new products based on an entirely new technology. The contrast agent will be the first nanoparticle-based injection preparation on the market. Lacking acceptance can therefore be a barrier. On the other hand there is an increasing interest for nanomaterial in biomedical applications so that can give the product extra publicity.

- Improved MRI technique

There is a risk that MRI technology evolves to a degree that most scans can be done without contrast agents. Pulse sequences that utilize the effects of contrast agents are also being developed and since imaging speed is improved with contrast agents it is difficult to predict which way the balance will tip during the next few decades.

- Competition with Customer

Since SPAGO Imaging AB turns to investors and licensees that already exist in the MRI contrast agent market, there may be a risk to compete with their own potential customers. One can imagine that these companies do not want to invest in SPAGO Imaging AB because it would reduce demand for their own existing products.

- Emergence of new substitutes

There is always a threat that substitutes with better sensitivity and specificity than MRI will be developed. However, since SPAGO's contrast agent enhances the existing MRI technology there is no need for new, expensive, equipment.

Hospitals certainly prefer a contrast agent that improves the existing technology than an entirely new technology that requires buying expensive equipments.

- The European Commission directive 2004/40/CE

When an MRI scan is being performed most of the staff members leave the room. However the main magnet is always on, so when the patient are being placed in the scanner or anaesthetized, the staff member is present in the magnetic field. Engineers are also exposed to the magnetic field whenever a scanner is being installed or serviced. The directive (2004/40/CE) is postponed to April 2012 and it is unclear whether the limits will apply to MRI, but if it does, albeit highly unlikely, it could end up preventing the technique from being used in Europe.

6.4 The Product Life Cycle

The product of SPAGO Imaging AB is today in a stage before the introduction phase, because the product is not yet launched on the market. The nearest stage is, however, the introduction phase so the company should start looking at the different strategies designed for this phase.

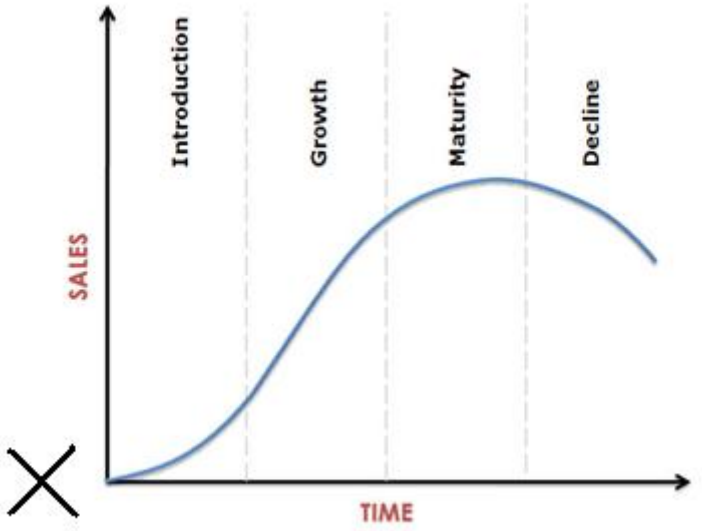


Figure 6.4 – SPAGO´s product is in a stage before the introduction phase,[333]

In the introduction phase it is important to create product awareness in the customers mind. It is also important to create a non-differentiated product. The product that SPAGO Imaging AB now is developing can be said to be non-differentiated because it can be applied in many different areas. There is an opportunity to attach different targeting molecules and create more differentiated products, targeted to specific segments, i.e. cancer types. However, according to the theory behind the product life cycle, it is good idea to first try to launch SPAGO´s original product without targeting molecules because otherwise the product becomes too differentiated and a too narrow market is created.

There are two well-known strategy options in the introduction phase: *skimming* or *penetrating*. Because of the high development costs and because high entry barriers exist (due to existing/future patent) I suggest the skimming strategy. The price of the product should therefore be relatively high.

[333] Homepage of NoteDesk, *The product life cycle* [Online] (Redrawn)

6.5 The Ansoff Matrix

Since SPAGO´s contrast agent is a new product and it will be launched on an already existing market (MRI for breast cancer) it can therefore be said to be a product development.

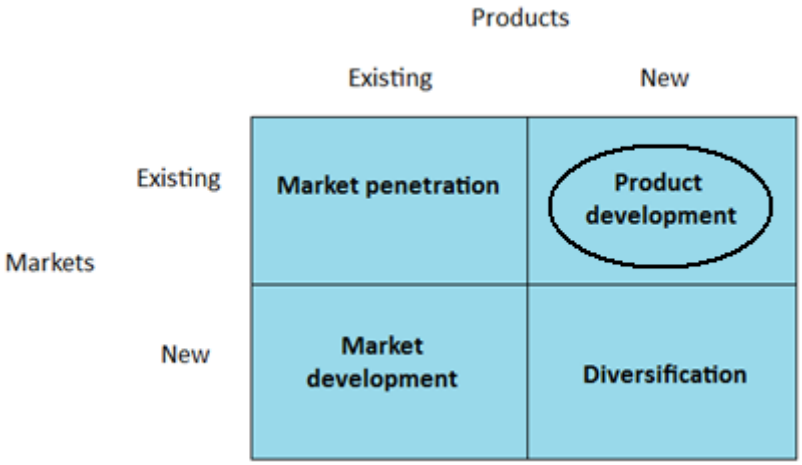


Figure 6.5 – The diversification strategy.

According to the theory there were three different way to conduct a product development: *product extension*, *product replacement* or *product innovation*. The product of SPAGO Imaging AB is based on a whole new technology and is therefore a product innovation. There were two different approaches for innovation: *technology push* or *market pull*. Because the product is entirely based on the knowledge created by the scientists at SPAGO Imaging AB, the approach can said to be a technology push.

One important thing regarding the technology push approach is to not lose the customer focus. The history is filled with examples of companies that have blindly pursued technological developments without regard to the real market needs. Therefore it is important that the company analyze the customers; who there are, their needs and their preferences, to maintain a customer focus.

7. Summary and Reflections

Chapter seven summarizes the impressions from the empirics and the analysis. The most important findings are brought together and form the basis of the presented recommendations for SPAGO Imaging AB.

The purpose of this thesis was to analyze the market of SPAGO Imaging AB´s product in the field of breast cancer. Both an analysis of the different methods used to screen and diagnose breast cancer and an analysis of SPAGO´s contrast agent was conducted.

The study has shown that mammography is the common method for screening the general population. The method is sometimes complemented with Breast Physical Examination to first see if any suspicious nodules can be found. For women with dense breast or when needing a second screening test, either sonography or MRI are used.

MRI is a powerful tool for finding signs of breast cancer because of its high sensitivity, but, as the analysis shows, the modality also has downsides in the form of a relatively high false-positive rate and the high cost per scan. Therefore, MRI is not appropriate as a screening test for the general population.

We are, however, likely to transition from a standardized screening, where all women undergo the same screening examination, i.e. mammography, to selection of a screening modality based on individual-risk. Women with increased risk need a more sensitive detection tool and because the MRI is the most sensitive screening method that exists today is the method also being recommended by the ACS.

Regarding the methods that are used to diagnose breast cancer, they can be said to have two different purposes. One purpose is to classify the tumor, to see if it's benign or malignant. For this role is biopsy the best method and no non-invasive test can compete with it today.

The other purpose of a diagnostic test is to determine size and location of the tumor and to see whether or not it has spread to the lymph nodes. For this

purpose mammography and sometimes sonography are being used, despite the fact that MRI probably would be a better alternative. Why MRI isn't used instead can be due to the low specificity or simply because it's a relatively new method and the advantages have not yet been recognized. However, MRI will certainly play an increasingly important role in the diagnosis of patients with breast cancer.

I believe that the use of SPAGO´s contrast agent, to obtain improved MR-images, will also play a great role for the increased utility of the MRI technology. The product will probably increase booth the sensitivity and the specificity of the MRI method.

The product will however not change the fact that the MRI is not appropriate for general screening, despite the fact that the specificity will increase. The reason the high cost together with the long waiting time after the administration of the contrast.

The potential market segments of SPAGO´s contrast agent is instead risk-group screening. It will be easier to find the women with increased risk as new and better tools are being developed and for these women the sensitivity of the test is the most important factor regarding screening tests. The MRI technology together with SPAGO´s new contrast agent will give a high sensitivity and therefore will more tumors be found in an early phase, leading to that more lives can be saved. SPAGO´s contrast agent will also increase the otherwise relatively low specificity, so that fewer people will be misdiagnosed. The products high cost would probably not create any major problem because earlier detection also means cheaper treatments.

As mentioned earlier, the MRI will play an increasingly important role in the diagnostics area, so this market segment is also very attractive. SPAGO´s contrast agent will give better images, so the exact location, size and shape can be determined in higher extent.

The most important opportunity, identified in the SWOT analysis, is the growing MRI market in the field of breast cancer. A growing MRI market leads to a more frequent use of MRI-contrast agents, which is a great opportunity to SPAGO Imaging AB. The most important threat is the fact that SPAGO´s contrast agent is nanoparticle-based, actually the first injection preparation based on nano-science. There is always a risk in new products based on an entirely new technologies,

lacking acceptance can therefore be a barrier. Therefore, it is important that the company clearly emphasizes the product's high safety.

An important opportunity is the ability to attach targeting molecules on the particles, creating what is referred to as molecular imaging. A contrast agent with a targeting function would probably have very high sensitivity and specificity and according to Christer Lundahl the price of such product could allows being very high, 20 000kr/dose (see Appendix D).[334] The ability to develop contrast agents with targeting functions from the platform technology will itself be a good selling point. Therefore, I believe that it is important for the company to point out this opportunity for potential investors.

Recommended future studies regarding marketing research for SPAGO´s contrast agent could be another cancer type, such as prostate cancer. Prostate cancer is the second most frequently diagnosed cancer in men and screening tests for this malignancy is today a hot topic, with different clinical trials taking place in many parts of the world. So there is a major potential that the MRI technology together with SPAGO´s contrast agent could be used as a prostate cancer screening test.

Another interesting application area could be pancreatic cancer. At present, there is no method for the early detection of this sort of cancer. Therefore are the 5-year relative survival rates only 5 %. Research is underway to identify better methods of early detection and MRI together with SPAGO´s contrast agent could perhaps be an option.

[334] Lundahl, C., personal communication, October 6, 2009

References

Bocks:

American Cancer Society (2007), *Breast Cancer Facts & Figures 2007-2008*, Atlanta: American Cancer Society, Inc.

American Cancer Society (2009), *Cancer Facts & Figures 2009*, Atlanta: American Cancer Society, Inc.

American Cancer Society & National Comprehensive Cancer Network (2006), *Breast Cancer - Treatment Guidelines for Patients*, Atlanta: American Cancer Society, Inc.

Andberg, L. & Eliasson, B. (2005), *Marknadsplanen – Praktisk handledning för marknadsplanerare*, Malmö: Liber

Andersen, I. (1998), *Den uppenbara verkligheten – Val av samhällsvetenskaplig metod*, Lund: Studentlitteratur

Armstrong, G. & Kotler, P. (2006), *Marketing – An Introduction,* New Jersey: Pearson Prentice Hall

Armstrong, G., Kotler, P., Saunders, J. & Wong, V. (2005), *Principles of Marketing*, New Jersey: Prentice-Hall

Björklund, M. & Paulsson, U. (2003), *Seminarieboken – att skriva, presentera och opponera*, Lund: Studentlitteratur

Bombardieri, E., Bonadonna, G. & Gianni, L. (eds.) (2008), *Breast Cancer - Nuclear Medicine in Diagnosis and Therapeutic Options*, Berlin, Heidelberg: Springer-Verlag Berlin Heidelberg

Boné, B. (1997), *Contrast Medium Enhanced Magnetic Resonance Imaging in Diagnosis of Breast Diseases,* Stockholm: Publisher missing

Bruening, W., Kostinsky, H., Launders, J., Pinkney, N., Schoelles, K. & Turkelson, C. (2006), *Comparative Effectiveness Review No. 2: Effectiveness of Noninvasive Diagnostic Tests for Breast Abnormalities,* Rockville, MD: Agency for Healthcare Research and Quality

Center, M., Garcia, M., Hao, Y., Jemal, A., Siegel, R., Thun, M. & Ward, E. (2007), *Global Cancer Facts & Figures 2007*, Atlanta: American Cancer Society (ACS)

Davidson, B. & Patel, R. (2003), *Forskningsmetodikens grunder – Att planera, genomföra och rapportera en undersökning*, Lund: Studentlitteratur

Denscombe, M. (2007), *The Good Research Guide: for small-scale social research projects*, Maidenhead: Open University Press

Eriksson, L. & Wiedersheim-Paul, F. (2006), *Att utreda, forska och rapportera*, Malmö: Liber

Hague, P. (2002), *Market Research – A guide to Planning, Methodology and Evaluating*, London: Kogan Page

Hayat, M. (ed.) (2008), *Methods of Cancer Diagnosis, Therapy and Prognosis Breast Carcinoma*, Dordrecht: Springer Netherlands

Hunt, K., Robb, G., Strom, E., & Ueno, N. (eds.), (2008), *Breast Cancer 2nd edition,* New York: Springer Science + Business Media

Höst, M., Regnell, B. & Runeson, P. (2006), *Att genomföra examensarbete*, Lund: Studentlitteratur

Jobber, D. (2006), *Principles and practice of marketing,* London*:* McGraw-Hill Education

Johannessen, A. & Tufte, P. (2003), *Introduktion till samhällsvetenskaplig metod*, Malmö: Liber

Johnson, G., Scholes, K. & Whittington, R. (2005), *Exploring Corporate Strategy*, Harlow: Financial Times Prentice Hall

Johnson, G., Scholes, K. & Whittington, R. (2008), *Exploring Corporate Strategy*, Harlow: Financial Times Prentice Hall

Kotler, P. (1999), *Kotlers marknadsföring – Att skapa, vinna och dominera marknader*, Malmö: Liber

Landström, H. & Löwegren, M. (eds.) (2009), *Entreprenörskap och företagsetablering – Från idé till verklighet*, Lund: Studentlitteratur

Last, J. & Porta, M. (2008), *A dictionary of epidemiology*, Oxford: Oxford University Press

Lehmann, D. & Winer, R. (2005), *Analysis for Marketing Planning*, New York: McGraw-Hill/Irwin

Lekvall, P. & Wahlbin, C. (2001), *Information för marknadsföringsbeslut*, Göteborg: IHM Publishing

Liberman, L. & Morris, E. (2005), *Breast MRI - Diagnosis and Intervention*, New York: Springer Science + Business Media

Lundahl, U., Skärvad, P.-H. (1999), *Utredningsmetodik för samhällsvetare och ekonomer,* Lund: Studentlitteratur

McQuarrie, E. (2006), *The Market Research Toolbox – A Concise Guide for Beginners*, Thousand Oaks: SAGE Publications, Inc.

Nystrand, A. (ed.) (2005), *Cancer i siffror: populärvetenskapliga fakta om cancer - dess förekomst, bot och dödlighet*, Stockholm: Cancerfonden & Socialstyrelsen

Olsson, J. & Skärvad, P.-H. (2003), *Företagsekonomi 100,* Malmö: Liber

Perolle, J. (1998), *Computers and Social Change: Information, Property, and Power* [e-book], Belmont: Wadsworth Publishing Company, Available at: http://www.ccs.neu.edu/home/perrolle/book/, [Accessed 27 August 2009]

Piercy, N. (2002), *Market-led Strategic Change: Transforming the Process of Going to Market*, Oxford: Butterworth-Heinemann

Ries, A. & Trout, J. (1985), *Positionering - Kampen om ditt medvetande*, Lund: Studentlitteratur

Rinck, P. (2003), *Magnetic Resonance in Medicine – The Basic Textbook of the European Magnetic Resonance Forum*, Berlin: ABW Wissenschaftsverlag

Robson, C. (2002), *Real world research - a resource for social scientists and practitioner-researchers*, Oxford: Blackwell Publishers

Socialstyrelsen (2007), *Cancer Incidence in Sweden 2006*, Stockholm: Socialstyrelsen

The BFP Project Biomonitoring Futures (2006), *Current Best Biomonitoring Practices*, Virginia: Institute for Alternative Futures

Wallén, G. (1996), *Vetenskapsteori och forskningsmetodik*, Lund: Studentlitteratur

World Health Organization & International Union Against Cancer (2005), *Global action against cancer*, Geneva: World Health Organization

Journals:

Abati, A., Danforth, D., Filie, A., Giusti, R., Greene, M., Loud, J., Nichols, K., Prindiville, S. & Thiébaut, A. (2009), *Ductal Lavage in Women from BRCA1/2 Families: Is There a Future for Ductal Lavage in Women at Increased Genetic Risk of Breast Cancer?*, Cancer Epidemiology, Biomarkers & Prevention, 18(4), pp. 1243-1251

Abdelgawad, M., Casper, R., Chen, J., Jebrail, M., Metalnikov, P., Mousa, N., Wheeler, A., & Yang, H. (2009), *Droplet-Scale Estrogen Assays in Breast Tissue, Blood, and Serum*, Science Translational Medicine, 1(1), p. 1ra2

Abraham, L., Aiello Bowles, E., Carney, P., Elmore, J., Miglioretti, D., Sickles, E., & Yankaskas, B. (2008)**,** *Accuracy of Short-Interval Follow-Up Mammograms by Patient and Radiologist Characteristics,* American Journal of Roentgenology, 190(5), pp. 1200-1208

Abu-Alfa, A., Cowper, S., Kanal, E. & Kuo, P. (2007), *Gadolinium-based MRI Contrast Agents and Nephrogenic Systemic Fibrosis*, Radiology, 242(3), pp. 647-649

Affleck, I., Cordiner, C., Gilbert, F., Hood, D., Mathieson, D. & Walker, L. (1998), *Breast screening: the psychological sequelae of false- positive recall in women with and without a family history of breast cancer*, European Journal of Cancer, 34(13), pp. 2010-2014

Akiyama, F., Furusawa, H., Hideyuki Wakamatsu, H., Ifuku, H., Matsu, T., Nakahara, H., Nakahara, M. Namba, K., Shirouzu, M., Tamura, S., Tanaka, C. & Watanabe, R. (2002), *Extension of Breast Cancer: Comparison of CT and MRI*, Radiation Medicine, 20(1), pp. 17-23

Alciati, M., Baines, C., Barton, M., Bobo, J., Coleman, C., Dolan, M., Gaumer, G., Hannan, J., Kopans, D., Kutner, S., Lane, D., Lawson, H., Meissner, H., Moorman, C., Osuch, J., Pennypacker, H., Pierce, P., Saslow, D., Sciandra, E., Smith, R. & Coates, R. (2004), *Clinical Breast Examination: Practical Recommendations for Optimizing Performance and Reporting,* CA: A Cancer Journal for Clinicians, 54(6), pp. 327-344

Alciati, M., McDonald, S. & Saslow, D. (2004), *Performance and reporting of clinical breast examination: a review of the literature*, CA: A Cancer Journal for Clinicians, 54(6), pp. 345-361.

Allison, C., Chen, F., Gao, D., Ray, R., Thomas, D. & Wang, W. (2002), *Randomized trial of breast self-examination in Shanghai: final results*, Journal of the National Cancer Institute, 94(19), pp. 1445-1457

Allison, K., De Paredes, E. & Smith, M. (2006), *Nonmammographic Evaluation of the Extent of Breast Carcinoma*, Seminars in ultrasound, CT, and MR, 27(4), pp. 308-319

Amalu, W. (2004), *Nondestructive Testing of the Human Breast: The Validity of Dynamic Stress Testing in Medical Infrared Breast Imaging*, Proceedings of the 26th Annual International Conference of the IEEE EMBS, pp. 1174-1177

Anderson, B., Anderson, M., Arias, R., Cazzaniga, M., Clark, R., Dooley, W., Elledge, R., Esserman, L., Euhus, D., Ganz, P., Haffty, B., Hung, D., Kass, F., Kelley, M., Khan, S., King, B., King, E., Kuerer, H., Ljung, B., Love, S., O'Shaughnessy, J., Page, D., Phillips, R., Quiring, J., Schmit, P., Troyan S. & Veronesi, U. (2001), *Ductal lavage for detection of cellular atypia in women at high risk of breast cancer***,** Journal of the national cancer institute, 93(21), pp. 1624-1632.

Anderson, S., Bryant, J., Deutsch, M., Fisher, B., Fisher, E., Leong, J.-H., Margolese, R. & Wolmark, N. (2002), *Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer*, The New England Journal of Medicine, 347(16), pp. 1233-1241

Andrews, K., Boetes, C., Burke, W., Harms, S., Leach, M., Lehman, C., Morris, E., Pisano, E., Russell, C. Saslow, D., Schnall, M., Sener, S., Smith, R., Warner, E. & Yaffe, M., (2007), *American Cancer Society Guidelines for Breast Screening with MRI as an Adjunct to Mammography*, CA: A Cancer Journal for Clinicians, 57(2), pp. 75-89

Andrews, V., Lilley, L., Radford, L., Rao, R. & Ulissey, M. (2009), *Axillary Staging by Percutaneous Biopsy: Sensitivity of Fine-Needle Aspiration Versus Core Needle Biopsy*, Annals of Surgical Oncology, 16(5), pp. 1170-1175

Aspelin, P., Boné, B., Isberg, B., Perbeck, L. & Veress, B. (1995), *Contrast-enhanced MR imaging of the breast in patiants with breast implants after cancer surgery*, Acta Radiologica, 36(2), pp. 111-116

Astrahan, M., Bernstein, L., Ma, H., Parisky, Y., Pike, M., Salane, M., Siozon, C., Ursin, G. & Wu, A., (2003), *Mammographic density and breast cancer in three ethnic groups*, Cancer Epidemiology, Biomarkers & Prevention, 12(4), pp. 332-338

Badawi, R., Boone, J., Borowsky, A., Bowen, S., Burkett, G., Chaudhari, A., Cherry, S., Fu, L., Hagge, R., Lindfors, K., Martinez, S., Packard, N., Qi, J., Shelton, D., Wu, Y. & Yang, K. (2009), *Initial Characterization of a Dedicated Breast PET/CT Scanner During Human Imaging*, Journal of Nuclear Medicine, 50(9), pp. 1401-1408

Baines, C., Miller, A., To, T., & Wall, C. (2000), *Canadian National Breast Screening Study-2: 13-Year Results of a Randomized Trial in Women Aged 50–59 Years*, Journal of the National Cancer Institute, 92(18), pp. 1490-1499

Baird, C., Bethke, K., Bryk, M., Khan, S., Ljung, BM., Morro, M. Nayar, R., Rademaker, A., Ramakrishnan, R., Rodriguez, N., Staradub, V., Wiley, E. & Wolfman, J. (2004), *Ductal Lavage Findings in Women With Known Breast Cancer Undergoing Mastectomy*, Journal of the National Cancer Institute, 96(20), pp. 1510-1517

Baker, L. & Baras, J. (2009), *Magnetic Resonance Imaging And Low Back Pain Care For Medicare Patients*, Health Affairs, 28(6), pp. w1133-w1140

Bellanova, B., Cacciari, N., Martoni, A., Pannuti, F., Strocchi E., Vecchi, F., Zamagni, C., & Zanichelli, L. (1995), *CEA, MCA, CA 15.3 and CA 549 and their combinations in expressing and monitoring metastatic breast cancer: a prospective comparative study*, European Journal of Cancer, 31(10), pp. 1615-1621

Benard, F. & Turcotte, E. (2005), *Imaging in breast cancer: Single-photon computed tomography and positron-emission tomography*, Breast Cancer Research, 7(4), pp. 153-162.

Berg, W. (2001), *Imaging the local extent of disease*, Seminars in Breast Diseases, 4, pp. 153-173

Berg, W., Bhargavan, M., Carter, B., Gutierrez, L., Ioffe, O., Lewis, R. & NessAiver, M. (2004), *Diagnosticaccuracy of mammography, clinical examination, ultrasound, and MR imaging in preoperative assessment of breast cancer*, Radiology, 233(3), pp. 830-849

Berg, W., Blume, J., Mendelson, E., Merritt, C., & Schleinitz, M. (2006), *Screening breast ultrasound in high-risk women*, American College of Radiology Imaging Network (ACRIN) [Online], 20 November, Available at: http://www.acrin.org/Portals/0/Protocols/6666/A6666partial_summary.pdf, [Accessed 17 October 2009]

Berlin, J., Bernstein, L., Burkman, R., Daling, J., Folger, S., Malone, K., Mandel, M., Marchbanks, P., McDonald, J., Norman, S., Simon, M., Spirtas, R., Strom, B., Ursin, G., Weiss, L., Wilson, H. & Wingo, P. (2002), *Oral contraceptives and the risk of breast cancer*, The New England Journal of Medicine, 346(26), pp. 2025-2032

Bieling, H., Huhn, W., Koenig, R., Kuhl, C., Leutner, C., Schild, H., Schrading, S. & Wardelmann, E. (2007), *MRI for diagnosis of pure ductal carcinoma in situ: a prospective observational study,* The Lancet, 370(9586), pp. 485-492

Birdwell, R., Daniel, B. & Ikeda, D. (2000), *Potential role of magnetic resonance imaging and other modalities in ductal carcinoma in situ detection*, Seminars in Breast Diseases, 3, pp. 50-60

Bissonauth, V., Fafard, E., Ghadirian, P., Maugard, C., Narod, S., Robidoux, A. & Shatenstein, B. (2009), Weight History, Smoking, *Physical Activity and Breast Cancer Risk among French-Canadian Women Non-Carriers of More Frequent BRCA1/2 Mutations*, Journal of Cancer Epidemiology, 2009, pp. 1-11

Bittner, N., DeMartini, W., Eby, P., Kim, J., Lehman, C., Loiselle, C., & Peacock, S. (2008), *Dynamic contrast enhanced MRI kinetics and invasive breast cancer: a potential prognostic marker for radiation therapy*, International Journal of Radiation Oncology, 72(1), p. S176

Bloch, F., Hanson, W. & Packard, M. (1946), *Nuclear induction*, Physical Review, 69, p. 127

Brandes, A., Bui, F., Feretti, G., Geatti, O., Lumachi, F., Marzola, C., Povolato, M. & Zucchetta, P. (2001), *Sestamibi scintimammography in pT1 breast cancer: alternative or complementary to X-ray mammography?,* Anticancer research, 21(3C), pp. 2201-2205

Brem, A. & Voigt, K.-I. (2009), *Integration of market pull and technology push in the corporate front end and innovation management-Insights from the German software industry*, Technovation, 29(5), pp. 351-367

Brodack, J., Katzenellenbogen, J., Mathias, C., McGuire, A., Mintun, M., Siegel, B. & Welch, M. (1988), *Breast cancer: PET imaging of estrogen receptors*, Radiology, 169(1), pp. 45-48

Brown, P., Chiarelli, A., Mai, V., Majpruz, V., Shumak, R., Thériault, M. (2009), *The Contribution of Clinical Breast Examination to the Accuracy of Breast Screening,* Journal of the National Cancer Institute, 101(18), pp. 1236-1243

Buck, A., Glatting, G., Guhlmann, A., Hörster, T., Koretz, K., Kreienberg, R., Kühn, T., Nüssle, K., Reske, S., Rieber, A., Santjohanser, C. & Schirrmeister, H. (2001), *Fluorine-18 2-deoxy-2-fluoro-D-glucose PET in the preoperative staging of breast cancer: comparison with the standard staging procedures*, European Journal of Nuclear Medicine and Molecular Imaging, 28(3), pp. 351-358

Burke, W., Costanza, M., Evans, P., Eyre, H., Foster, R., Hendrick, E., Saslow, D., Sawyer, K., Sener, S. & Smith, R. (2003), *American Cancer Society guidelines for breast cancer screening: Update 2003*, CA: A Cancer Journal for Clinicians, 53(3), pp. 141-169

Camacho, M., Hui, F. & Parker, M. (2005), *Female Breast Radiation Exposure During CT Pulmonary Angiography*, American Journal of Roentgenology, 185(5), pp. 1228-1233

Carson, P., Engle, K., Fowlkes, B., Hunt, K., Johnson, T., Krücker, J., LeCarpentier, G., Paramagul, C., Roubidoux, M. & Thorson, N. (2008), *Suspicious Breast Lesions: Assessment of 3D Doppler US Indexes for Classification in a Test Population and Fourfold Cross-Validation Scheme*, Radiology, 249(2), pp. 463-470

Changlassian, T. & Dershaw, D. (1989), *Mammography after prosthesis placement for augmentation or reconstructive mammoplasty,* Radiology, 170(1), pp. 69-74

Collaborative Group on Hormonal Factors in Breast Cancer (1996), *Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,239 women without breast cancer from 54 epidemiological studies*, The Lancet, 347(9017), pp. 1713-1727.

Corino, G. & French, P. (2008), *Diagnosis of breast cancer by X-ray diffraction of hair*, International Journal of Cancer, 122(4), pp. 847-856

DeMartini, W., Lehman, C., Partridge, S., Peacock, P. & Wang, L. (2009), *MRI-Detected Suspicious Breast Lesions: Predictive Values of Kinetic Features Measured by Computer-Aided Evaluation*, American Journal of Roentgenology, 193(3), pp. 826-831

Dunham, W. (2008), *New breast cancer screening test will use saliva,* Breastcancer.org [Online], 10 January, Available at: http://www.breastcancer.org/symptoms/testing/new_research/20080110.jsp, [Accessed 17 October 2009]

Early Breast Cancer Trialists' Collaborative Group (2000), *Favourable and unfavourable effects on long-term survival of radiotherapy for early breast cancer: an overview of the randomised trials*, The Lancet, 355(9217), pp. 1757-1770

Engelmark Cederborg, S. (2006), *Partiklar med potential*, Forskning & Medicin, 4, [Online] 19 December, Available at: http://forskningochmedicin.vr.se/knappar/tidigarenummer/innehallnr42006/partiklarmedpotential.4.28a3695010f65c9aeac80001906.html, [Accessed 17 October 2009]

Forrest, W. (2009), *PET/MRI breast imaging prototype shows early promise*, AuntMinnie [Online], 16 June, Available at: http://www.auntminnie.com/index.asp?Sec=sup&Sub=mri&Pag=dis&ItemId=86227, [Accessed 17 October 2009]

Fox, M. (2007), *New recommendations call for MRI in breast cancer*, Breastcancer.org [Online], 28 Mars, Available at: http://www.breastcancer.org/symptoms/testing/new_research/20070328b.jsp, [Accessed 17 October 2009]

Francis, J., Haberman, J. & Love, T. (1980), *Screening a Rural Population for Breast Cancer Using Thermography and Physical Examination Techniques: Methods and Results-A Preliminary Report*, Annals of the New York Academy of Sciences, 335(1), pp. 492-500

Freedonia Group (2004), *Medical Imaging Equipment in the United States to 2008*, pp. 1-5

Gøtzsche, P. & Kösters, J. (2009), *Regular self-examination or clinical examination for early detection of breast cancer*, *The Cochrane Library* 2009, 3 [Online] Available at: http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003373/pdf_fs.html, [Accessed 17 October 2009]

Gøtzsche, P. & Olsen, O. (2000), *Is screening for breast cancer with mammography justifiable?,* The Lancet*,* 355(9198), pp. 129-134

Herbillon, G. (2007), *Introduction to the EC Directive 2004/40/CE – Obligations of employers (risk assessment, protective measures, worker information and training*) [Online], Available at: http://www.icnirp.de/Joint/HerbillonAbstract.pdf, [Accessed 17 October 2009]

Hylton, N. (2005), *Magnetic Resonance Imaging of the Breast: Opportunities to Improve Breast Cancer Management*, Journal of Clinical Oncology, 23(8), pp. 1678-1684

Imaginis Report (2001), *Nuclear Medicine Breast Cancer Test May Be Helpful for Some Women, Particularly in Those with Dense Breasts*, Imaginis Report [Online], September, Available at: http://www.imaginis.com/breasthealth/news/news9.19.01.asp, [Accessed 17 October 2009]

Kahn, M. (2007), *Simple test may help predict breast cancer return*, Breastcancer.org [Online], 24 September, Available at: http://www.breastcancer.org/symptoms/testing/new_research/20070924.jsp, [Accessed 17 October 2009]

Kashiki, Y., Kawaguchi, Y., Nagao, Y., Saji, S. & Sugiyama, Y. (2003), *Relationship between mammographic density and the risk of breast cancer in Japanese women: a case-control study*, Breast Cancer, 10(3), pp. 228-233

Knutson, D. & Steiner, E. (2007), *Screening for Breast Cancer: Current Recommendations and Future Directions*, American Family Physician, 75(11), pp. 1660-1666

Le Bihan, D. (2009), *Threats to ultrahigh-field MRI in Europe*, Physicsworld [Online], Juli, Available at: http://physicsworld.com/cws/article/print/39950, [Accessed 17 October 2009]

Lindsey, H., 2001, *Ductal lavage offers new screening option for breast cancer*, The Lancet Oncology, 2(2), p. 70

Lister-Sharp, D., Petticrew, M. & Sowden, A. (2001), *False-negative results in screening programs*, International Journal of Technology Assessment in Health Care, 17(2), pp. 164-170

Loncar, D. & Mathers, C. (2006), *Projections of global mortality an burden of disease from 2002 to 2030*, PLoS Medicine, 3(11), pp. 2011-2030

Maggi, C., Messineo, D., Potente, G. & Savelli, S. (2009), *Practical application of contrast-enhanced magnetic resonance mammography [CE-MRM] by an algorithm combining morphological and enhancement patterns*, Computerized Medical Imaging and Graphics, 33(2), pp. 83-90

Masha, Z. (2002), *Medical Imaging*, BCC Research, Report Code: HLC020B

Orel, S. & Schnall, M. (2001), *MR imaging of the breast for the detection, diagnosis, and staging of breast cancer*, Radiology, 220(1), pp. 13-30

Pound, R., Purcell, E. & Torrey, H. (1946), *Resonance absorption by nuclear magnetic moments in a solid*, Physical Review, 69, pp. 37-38

Richwine, L. (2007), *U.S. OKs test to predict breast cancer return, Breastcancer.org* [Online], 6 February, Available at: http://www.breastcancer.org/symptoms/testing/new_research/20070206.jsp, [Accessed 10 November 2009]

Ridley, E. (2009), *Automated whole-breast US doubles cancer detection*, AuntMinnie [Online], 10 September, Available at: http://www.auntminnie.com/index.asp?Sec=sup&Sub=wom&Pag=dis&ItemId=87198, [Accessed 10 November 2009]

Sarasvathy, S. (2001), *Causation and Effectuation: Toward a Theoretical Shift from Economic Inevitability to Entrepreneurial Contingency*, The Academy of Management Review, 26(2), pp. 243-263

Sayewitz, R. (2002), *Jupiter Medical buys digital mammography machine,* South Florida Business Journal [Online], Available at: http://southflorida.bizjournals.com/southflorida/stories/2002/05/13/focus2.html, [Accessed 10 November 2009]

Smith, J. (2005), *Molecular Imaging Agents and Systems – A Market Briefing,* Kalorama Information

Stokes, D. (2000), *Entrepreneurial marketing – A conceptualization from qualitative research*, Qualitative Market Research, 3(1), pp. 47-54

The, W. & Wilson, A. (1998), *The role of ultrasound in breast cancer screening. A consensus statement by the European Group for Breast Cancer Screening*, European Journal of Cancer, 34(4), pp. 449-450

Yee, K. (2009), *Oregon case spotlights clinical validity of breast thermography*, AuntMinnie [Online], 25 May, Available at: http://www.auntminnie.com/index.asp?Sec=sup&Sub=imc&Pag=dis&ItemId=85857, [Accessed 10 November 2009]

Zebrowski, M. (2007), *The Cancer Market Outlook to 2012*, Business Insights Ltd

Internet Sources:

Homepage of About.com, *Breast Ultrasound - Imaging for Breast Abnormalities*, Available at: http://breastcancer.about.com/od/diagnosis/a/ultrasound.htm, [Accessed 2009-09-28]

Homepage of About.com, *Tumor Marker Test Overview – Breast Cancer Tumor Marker Tests*, Available at: http://breastcancer.about.com/od/diagnosis/p/tumor_mkr_ov.htm, [Accessed 2009-10-05]

Homepage of Accelerator Nordic AB, *Om Accelerator*, Available at: http://www.acceleratorab.se/about.aspx, [Accessed 2009-08-19]

Homepage of American Cancer Society, *Tumor Markers*, Available at: http://www.cancer.org/docroot/PED/content/PED_2_3X_Tumor_Markers.asp?sitearea=PED#Whats_new_in_tumor_marker_research, [Accessed 2009-10-05]

Homepage of American Society of Clinical Oncology (ASCO), *Understanding Tumor Markers*, Available at: http://www.cancer.net/patient/All+About+Cancer/Cancer.Net+Features/Treatments%2C+Tests%2C+and+Procedures/Understanding+Tumor+Markers?cpsextcurrchannel=1, [Accessed 2009-10-05]

Homepage of AuntMinnie.com, *Refurbished MRI biggest competition to new systems*, Available at: http://www.auntminnie.com/index.asp?Sec=sup&Sub=bai&Pag=dis&ItemId=81982, [Accessed 2009-10-08]

Homepage of Breastcancer.org, *Biopsy,* Available at: http://www.breastcancer.org/symptoms/testing/types/biopsy.jsp, [Accessed 2009-10-02]

Homepage of Breastcancer.org, *Blood Marker Tests,* Available at: http://www.breastcancer.org/symptoms/testing/types/blood_marker.jsp, [Accessed 2009-10-06]

Homepage of Breastcancer.org, *Breast Physical Exam*, Available at: http://www.breastcancer.org/symptoms/testing/types/physical_exam.jsp, [Accessed 2009-09-21]

Homepage of Breastcancer.org, *CT (CAT) Scans*, Available at: http://www.breastcancer.org/symptoms/testing/types/cat_scans.jsp, [Accessed 2009-10-07]

Homepage of Breastcancer.org, *Mammograms*, Available at: http://www.breastcancer.org/symptoms/testing/types/mammograms/, [Accessed 2009-09-17]

Homepage of Breastcancer.org, *Mammography: Benefits, Risks, What You Need to Know,* Available at: http://www.breastcancer.org/symptoms/testing/types/mammograms/benefits_risks.jsp, [Accessed 2009-09-17]

Homepage of Breastcancer.org, *Mammography Technique and Types,* Available at: http://www.breastcancer.org/symptoms/testing/types/mammograms/types.jsp, [Accessed 2009-09-17]

Homepage of Breastcancer.org, *New scans prompt mastectomies for breast patients*, Available at: http://www.breastcancer.org/symptoms/testing/new_research/20080516b.jsp, [Accessed 2009-10-15]

Homepage of Breastcancer.org, *Oncotype DX Test*, Available at: http://www.breastcancer.org/symptoms/testing/types/oncotype_dx.jsp, [Accessed 2009-10-04]

Homepage of Breastcancer.org, *Scan could do away with mammogram pain*, Available at: http://www.breastcancer.org/symptoms/testing/new_research/20061128.jsp, [Accessed 2009-10-09]

Homepage of Breastcancer.org, *Thermography*, Available at: http://www.breastcancer.org/symptoms/testing/types/thermography.jsp, [Accessed 2009-09-30]

Homepage of Breastcancer.org, *Ultrasound*, Available at: http://www.breastcancer.org/symptoms/testing/types/ultrasound.jsp, [Accessed 2009-09-28]

Homepage of Breastcancer.org, *Whole-Body PET Scans Have High False Positive Rates for Breast Cancer*, Available at: http://www.breastcancer.org/symptoms/testing/new_research/20060719.jsp, [Accessed 2009-10-10]

Homepage of Breastthermography.com, *Case Studies,* Available at: http://www.breastthermography.com/case_studies.htm, [Accessed 2009-10-10]

Homepage of Breastthermography.com, *What is the Procedure Like*, Available at: http://www.breastthermography.com/breast_thermography_proc.htm, [Accessed 2009-09-30]

Homepage of Doctors Guide, *MRI Contrast Agent Linked to Rare Disease*, Available at: http://www.docguide.com/news/content.nsf/news/852571020057CCF68525726E006681B9, [Accessed 2009-10-19]

Homepage of Emory University, *Cancer Diagnosis: Core Needle Biopsy (CNB),* Available at: http://www.cancerquest.org/index.cfm?page=3704, [Accessed 2009-09-29]

Homepage of Imaginis, *Nuclear Medicine Breast Imaging (Scintimammography*), Available at: http://www.imaginis.com/breasthealth/nuc_med.asp, [Accessed 2009-10-09]

Homepage of Imaginis, *Digital Mammography,* Available at: http://www.imaginis.com/breasthealth/digital_mammo.asp, [Accessed 2009-09-25]

Homepage of MedicineNet.com, *Cancer Detection & Treatment*, Available at: http://www.medicinenet.com/cancer_detection/article.htm, [Accessed 2009-10-10]

Homepage of Modular Healthcare Facilities, *MRI picture*, Available at: http://modularhealthcarefacilities.files.wordpress.com/2009/05/mri.jpg, [Accessed 2009-09-01]

Homepage of National Cancer Institute, *About the tool,* Available at: http://www.cancer.gov/BCRISKTOOL/about-tool.aspx#gail, [Accessed 2009-09-18]

Homepage of National Institute of Biomedical Imaging and Bioengineering (NBIB), *Dedicated Breast CT Scanner Offers Alternative to Mammography*, Available at: http://www.nibib1.nih.gov/HealthEdu/eAdvances/29Apr08, [Accessed 2009-10-12]

Homepage of New Choice Health – Medical Cost Comparison, *Breast Ultrasound Cost*, Available at: http://www.newchoicehealth.com/Directory/Procedure/58/Breast%20Ultrasound, [Accessed 2009-10-02]

Homepage of NoteDesk, *The product life cycle*, Available at: http://notesdesk.com/wp-content/uploads/2009/03/product-life-cycle-stages-plc.jpg, [Accessed 2009-11-06]

Homepage of Praktiskmedicin, *Rekommendationer*, Available at: http://www.praktiskmedicin.com/sjukdom.asp?sjukdid=848, [Accessed 2009-09-20]

Homepage of Radiological Society of North America (RSNA), *New Breast Imaging Technology Targets Hard-to-Detect Cancers*, Available at: http://www.rsna.org/media/rsna/rsna08_newsrelease_target.cfm?id=391, [Accessed 2009-10-27]

Homepage of RadiologyInfo, *Breast Ultrasound,* Available at: http://www.radiologyinfo.org/en/info.cfm?pg=breastus, [Accessed 2009-09-29]

Homepage of RadiologyInfo, *MRI of the Body (Chest, Abdomen, Pelvis)*, Available at: http://www.radiologyinfo.org/en/info.cfm?pg=bodymr, [Accessed 2009-09-07]

Homepage of RadiologyInfo, *Image Gallery – Breast Ultrasound*, Available at: http://www.radiologyinfo.org/en/photocat/gallery3.cfm?pid=1&Image=hi_us-system4.jpg&pg=breastus, [Accessed 2009-09-28]

Homepage of RadiologyInfo, *Safety*, Available at: http://www.radiologyinfo.org/en/safety/index.cfm?pg=sfty_xray#3, [Accessed 2009-11-12]

Homepage of SPAGO Imaging AB, *Home*, Available at: http://www.spagoimaging.se, 2009-08-23

Homepage of The Breast Center of Northwest Arkansas, *Ultrasound*, Available at: http://www.breastcenternwa.com/images/ultrasound.jpg, [Accessed 2009-09-28]

Homepage of The International Center for Nephrogenic Fibrosing Dermopathy Research (ICNFDR), *NSF – what is it?* Available at: http://www.icnfdr.org/, [Accessed 2009-10-13]

Homepage of The New York Times, *Mammography*, Available at: http://graphics8.nytimes.com/images/2007/08/01/health/adam/17085.jpg, [Accessed 2009-10-17]

Homepage of Therma Screen, *Thermography*, Available at: http://www.thermascreen.com/faq.html, [Accessed 2009-09-30]

Homepage of Top News, CT figure, Available at: http://www.topnews.in/health/files/Cone-beam-breast-CT.jpg, [Accessed 2009-10-08]

Homepage of UC Davis Health System, *Biopsy figure,* Available at: http://www.ucdmc.ucdavis.edu/pathology/images/ap/ap_sp_biopsy_fig1.jpg, [Accessed 2009-09-04]

Homepage of University of Windsor, *Applications of MRI*, Available at: http://web2.uwindsor.ca/courses/physics/high_schools/2006/Medical_Imaging/mriapplication.html, [Accessed 2009-10-01]

Homepage of WebMD*, Breast Ultrasound*, Available at: http://women.webmd.com/breast-ultrasound, [Accessed 2009-10-01]

Homepage of WebMD, *Oncotype DX Test for Breast Cancer*, Available at: http://www.webmd.com/breast-cancer/oncotype-dx-test-breast-cancer, [Accessed 2009-10-07]

Homepage of World Culture Pictorial, CT figure, Available at: http://www.worldculturepictorial.com/images/content/ct-scan.jpg, [Accessed 2009-10-07]

Personal Contacts and e-mails

Axelsson, O., personal communication, August 17, September 8, October 10, 2009

Lundahl, C., personal communication, October 6, 2009

Axelsson, O., 2009 [e-mail] Message to Rönnholm, A., Sent Wednesday 12 August, 13.14.

Axelsson, O., 2009 [e-mail] Message to Rönnholm, A., Sent Tuesday 3 November, 12.44.

Johansson, A., 2009 [e-mail] Message to Rönnholm, A., Sent Monday 16 November, 14.26.

Rönnow, K., 2009 [e-mail] Message to Rönnholm, A., Sent Monday 16 November, 12.09.

Appendix A – The Questionnaire

1. När används MRI idag när det gäller bröstcancer?
2. Vad tycker Ni det finns för fördelar och nackdelar med MRI?
3. Finns det några problem/nackdelar idag med de kontrastmedel för MRI som finns ute på marknaden?
4. Vilka önskemål har Ni gällande nya kontrastmedel inom MRI?

Nedanför beskrivs tre olika kontrastmedel (P1, P2 och p3). Läs igenom dessa produktbeskrivningar och svara sedan på frågorna 5-6.

P1

Pris = 200 kr/ dos

Säkerhet = 1 % risk för allvarlig biverkning* gfr<60 mL/min/1.73m^2

Sensitivitet= tumörer > 5mm 90 %

Specificitet= tumörer > 5mm 70 %

P2

Pris = 3000 kr/ dos

Säkerhet = 1 % risk för allvarlig biverkning* gfr<60 mL/min/1.73m^2

Sensitivitet= tumörer > 2mm 90 %

Specificitet= tumörer > 2mm 90 %

P3

Pris = 20 000 kr/ dos

Säkerhet = <1 % risk för allvarlig biverkning* gfr<60 mL/min/1.73m^2

Sensitivitet= tumörer > 2mm 95 % (30 % subgrupp ty HER2 typ allvarlig)

*Allvarlig biverkning betyder behov av sjukhusvistelse.

5. Vilket kontrastmedel skulle du ge till följande patientgrupp och varför?

a) Populations screening (kvinnor mellan 50 och 69 år)

☐ P1 ☐ P2 ☐ P3

b) Unga kvinnor med kompakt bröstvävnad

☐ P1 ☐ P2 ☐ P3

c) Kvinnor som har en släkting av första generationen (mor, syster, dotter) som har/haft bröstcancer

☐ P1 ☐ P2 ☐ P3

d) Kvinnor som har haft bröstcancer tidigare

☐ P1 ☐ P2 ☐ P3

e) Kvinnor som enligt genetisk profilering har 25 % eller högre ökad risk för bröstcancer

☐ P1 ☐ P2 ☐ P3

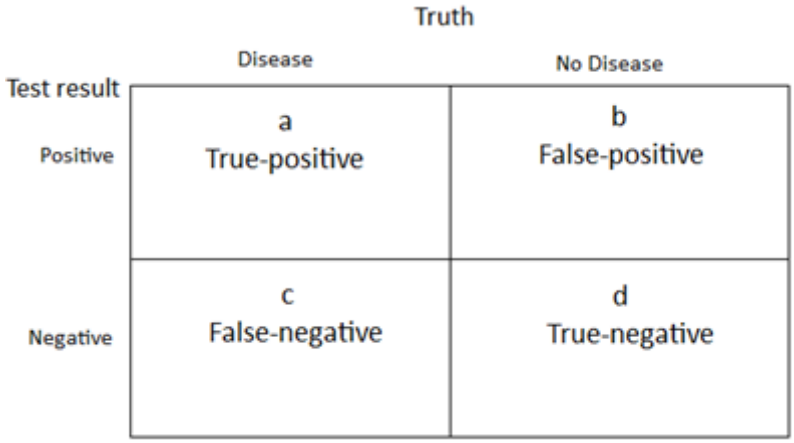
f) Kvinnor 70 år och äldre

☐ P1 ☐ P2 ☐ P3

6. Är det någon av dessa tre kontrastmedel som skulle göra att användandet av kontrastmedel skulle öka och i så fall varför?

Appendix B – Explanation of the Concepts Sensitivity and Specificity

Consider a test that only has two outcomes; positive or negative. Four possible scenarios can then occur.



Sensitivity represents the proportion of truly diseased persons in a population who are identified as being diseased by the test. It is a measure of the probability of correctly diagnosing a condition. Sensitivity is calculated as follows:[335]

$$Sensitivity = \frac{True\_positives}{True\_positives + False\_negatives} = \frac{a}{a + c}$$

Specificity of a test is defined as the percentage of persons without the disease of interest who have negative test results. It is a measure of the probability of correctly identifying a non-diseased person. Specificity is calculated as follows:[336]

$$Specificity = \frac{True\_negatives}{True\_negatives + False\_positives} = \frac{d}{d + b}$$

[335] Last, J., Porta, M., 2008, p. 227
[336] Last, J., Porta, M., 2008, p. 227

Besides worrying about being diagnosed with breast cancer, a false positive means more tests and follow-up visits, which can cause psychological stress and anxiety.[337] False negatives cause critical delays in diagnosis and treatment.[338]

[337] Affleck, I., Cordiner, C., Gilbert, F., Hood, D., Mathieson, D. & Walker, L., 1998, p. 2010
[338] Lister-Sharp, D., Petticrew, M. & Sowden, A., 2001, p. 164

Appendix C – Future Techniques for Breast Cancer Detection

A complemented analysis of future techniques for breast cancer detection has been conducted. Segmentation of the future techniques has been conducted in the same way as for the current techniques. The techniques have been divided into two segments: *screening tests* and *diagnostic tests*.

Segment	Tests
Screening tests	Speed-Weighted 3-D Power Doppler Ultrasound Hair Sample Saliva Cone Beam Breast Computed Tomography scanner Risk prediction tools
Diagnostic tests	Breast PET/CT Scanner PET/MRI Hybrid Tumor Markers

Screening Tests

Speed-Weighted 3-D Power Doppler Ultrasound

Sonography plays an important role in the assessment of suspect lesions viewed on mammograms. However, the accuracy of the technique is limited due to the significant number of false-positive results. The *Speed-weighted 3-D power Doppler ultrasound* represents a novel approach for more accurate detection of breast cancer. The method gives three-dimensional pictures of the breast and enables evaluation of breast tumor blood flow, analysis of the distribution of blood vessels, and quantitative measurement of blood flow velocity waveforms. A study with 78 women shows that the method has 100% sensitivity and 86% specificity.[339]

The Speed-weighted 3-D power Doppler ultrasound is launched on the market, but so far the product is not fully accepted, probably because of the lack of studies to ensure the technology's ability. Only one study has been conducted and it showed both high sensitivity and high specificity. The study was however very

[339] Carson, P., Engle, K., Fowlkes, B., Hunt, K., Johnson, T., Krücker, J., LeCarpentier, G., Paramagul, C., Roubidoux, M. & Thorson, N., 2008, pp. 463-470

small, so further evaluations are necessary to determine the correct values. It is difficult to comment on how the future of the technology will be without knowing the methods´ accuracy, but it will probably take over the role of Sonography, namely to screen young women with dense breasts.

Hair Sample

Scientists think that breast cancer might change hair's chemistry or the hair's follicle. A small study suggests that a special type of x-ray test (alpha-keratin diffraction pattern) done on hair found a unique ring pattern in the hair of women with breast cancer. However, the x-ray test wasn't perfect. One woman (out of 13) diagnosed with breast cancer didn't have the ring pattern in her hair and three women (out of 20) who didn't have breast cancer did have the ring pattern in their hair.[340]

The hair sample method is probably cheaper (per scan) than the existing techniques used today, but since the technology has both low sensitivity and specificity it´s highly unlikely that the method will be used in any large extent.

Saliva

Scientists in the United States are developing a screening test for breast cancer that checks a woman's saliva for evidence of the disease. They have identified 49 proteins in saliva that the screening test would track to distinguish healthy women from those with breast cancer. The focus is to launch the product as a screening tool in developing countries because mammograms are too expensive in these markets. The product is still in a development stage and no values for sensitivity and specificity are available.[341]

The saliva method is also unlikely to pose any threat to the existing screening methods, because it is not likely that the test will get accurate sensitivity and specificity parameters. The method will especially not be a threat to the MRI technology, because it is directed to those markets that cannot afford the MRI equipment.

[340] Corino, G. & French, P., 2008, p. 847
[341] Dunham, W., 2008, [Online]

Cone Beam Breast Computed Tomography Scanner

The Cone Beam Breast Computed Tomography scanner is a new kind of test to screen for breast cancer. Researchers believe that this new breast imaging technique will make breast cancers easier to see in dense breast tissue and will make breast screening more comfortable. The cost will be significantly more than a traditional mammogram. Right now, the Cone Beam system is available only for research purposes so no values for sensitivity and specificity are available.[342]

It is difficult to evaluate the Cone Beam Breast Computed Tomography scanner because it is in an early development phase where no data of sensitivity or specificity is available. One major drawback is that the technique will have a high cost.

Risk Prediction Tool

Risk prediction tools are not screening test, they do not detect cancer, but they can be said to belong to the category any way. The function of the tests is to find individuals at high risk for developing breast cancer so that these people get their screening tests more often and maybe get screened with more sensitive tests.

Today there are a few tools available to evaluate a person's risk of developing cancer. One test is the *Gail model*. The Gail model uses a woman's own personal medical history (number of previous breast biopsies and the presence of atypical hyperplasia in any previous breast biopsy tissue), her own reproductive history (age at the start of menstruation and age at the first live birth of a child) and the history of breast cancer among her first-degree relatives to estimate her specific risk of developing breast cancer.[343]

Scientists at the University of Toronto have also developed a new technique based on *digital micro fluidics*, where tiny droplets of fluid are manipulated electrically on the surface of a microchip. The technique measure the Estrogen level, which is a key hormone in human reproductive physiology, controlling ovulation and secondary sexual characteristics. The concentration of Estrogen and its

[342] Homepage of Breastcancer.org, *Scan could do away with mammogram pain* [Online]
[343] Homepage of National Cancer Institute, About the tool [Online]

metabolites in breast tissue are known to be increased in breast cancer patients compared to healthy women.[344]

Diagnostic Tests

Breast PET/CT Scanner

Researchers from the University of California, Davis (UCD) have constructed a dedicated breast PET/CT scanner, which will combine the sensitivity of PET imaging with the anatomical localization capabilities of CT.[345,346] The device is fully three-dimensional. Therefore, the method doesn't have the shadowing problem of 2D images. Shadowing can be problematic with mammography in patients with breast implants, because the implant will cover the cancer and make it difficult to visualize. Only four women have been imaged so the sensitivity and specificity could not be analyzed.[347]

The breast PET/CT scanner is expected to have a high sensitivity and specificity. The method also exposes the patient to a large dose of radiation and probably has a significantly high cost. Because of these drawbacks, the method is unlikely to pose any major threat to the existing diagnostic tests.

PET/MRI Hybrid

Researchers at Stony Brook University in New York are working to develop a high-resolution PET imaging system that can work inside an MRI scanner. The goal is to combining the MRI's high-resolution anatomic images with quantitative biochemical information from PET. The combination of these two pieces will, according to Bosky Ravindranath, research assistant and lead author of a study, lead to better diagnosis, staging and evaluation of breast cancer. A prototype has

[344] Abdelgawad, M., Casper, R., Chen, J., Jebrail, M., Metalnikov, P., Mousa, N., Wheeler, A., & Yang, H., 2009, p. 1ra2
[345] Badawi, R., Boone, J., Borowsky, A., Bowen, S., Burkett, G., Chaudhari, A., Cherry, S., Fu, L., Hagge, R., Lindfors, K., Martinez, S., Packard, N., Qi, J., Shelton, D., Wu, Y. & Yang, K., 2009, pp. 1401-1408
[346] Benard, F. & Turcotte, E., 2005, p. 154
[347] Badawi, R., Boone, J., Borowsky, A., Bowen, S., Burkett, G., Chaudhari, A., Cherry, S., Fu, L., Hagge, R., Lindfors, K., Martinez, S., Packard, N., Qi, J., Shelton, D., Wu, Y. & Yang, K., 2009, pp. 1401-1408

been built, but it´s only for rats because the prototype has an inner diameter of 145 mm and an axial length of 96 mm.[348]

The new PET/MRI technology is at a very early stage of development so how accurate the method will be in the end is difficult to say. The method is a threat to the traditional MRI technique but is not necessarily a bad thing for SPAGO Imaging AB, because it is possible that the new method also need contrast agents.

Tumor Markers

Researchers are starting to focus on genetic markers to detect cancer. Most cancers have changes in their DNA, so by looking for DNA changes in blood, stool or urine, scientists may be able to find cancers very early. The study of patterns of DNA changes (known as *genomics*) is likely to prove more useful than looking for single DNA changes. This new testing methods are still in the early stages of development. [349]

Another new approach is called *proteomics*. This technology looks at the patterns of all the proteins in the blood instead of looking at individual protein levels. Two blood tests have already been developed, Oncotype DX™ and MammaPrint®.[350]

The Oncotype DX test analyzes 21 specific genes in breast tumor sample. The test can predict the likelihood that invasive breast cancer will return or if the patient would benefit from chemotherapy.[351, 352] The test results in a so called *Recurrence Score*, a number between 0 and 100 that shows the risk of the breast cancer returning within 10 years of the original diagnosis. If the Recurrence Score are 18 or less the risk is said to be low, if the score is 31 or more the risk is high and if the score is 19 to 30 then the recurrence risk is said to be intermediate.[353]

The MammaPrint measures the activity of 70 genes. The test accurately picked which women were at low risk at least 90 percent of the time. Conversely, for

[348] Forrest, W., 2009, PET/MRI breast imaging prototype shows early promise, AuntMinnie, June 16 [Online]
[349] Homepage of American Cancer Society, Tumor markers [Online]
[350] Homepage of American Cancer Society, Tumor Markers [Online]
[351] Homepage of Breastcancer.org, Oncotype DX Test [Online]
[352] Homepage of WebMD, Oncotype DX Test for Breast Cancer [Online]
[353] Homepage of WebMD, Oncotype DX Test for Breast Cancer [Online]

women who were told they were at high risk for a recurrence within five years, just 23 percent actually had their cancer come back.[354]

Both of these tests are relatively new and have been tested on relatively small groups of women. Both tests cost more than $3,000.[355]

The proteomics method is an interesting future technique. Research and development are in progress, but the tests that are available today (Oncotype DX™ and MammaPrint®) are both too expensive and have too many false positive to really pose any threat to the existing diagnostic methods.

[354] Richwine, L., 2007, U.S. OKs test to predict breast cancer return, Breastcancer.org [Online]
[355] Kahn, M., 2007, Simple test may help predict breast cancer return, Breastcancer.org [Online]

Appendix D – Interview with Christer Lundahl, 2009-10-06

Vad finns det för fördelar och nackdelar med MRI?

- MRI är överlägsen jämfört med CT och konventionell röntgen när det gäller mjukvävnad. Mycket känsligare när det gäller att differentiera vävnad.
- MRI innebär ingen röntgenstrålning.
- Man kan eftergranska. Det kan man inte med ultraljud på samma sätt.
- Man kan använda tekniken på unga kvinnor (ju yngre kvinnor ju tätare bröst). Mammografi fungerar inte lika bra på täta bröst.

- MRI är dyrare och tar längre tid än mammografi.
- MRI är inte bra på kalk, det är däremot mammografi bra på.
- Organisatoriskt svårt att screena eftersom injektion av kontrastmedel måste ske innan MRI.

När används MR idag när det gäller bröstcancer?

- Används i unga patienter då deras bröst har en hög täthet av körtelvävnad jämfört med äldre kvinnor.
- Används när man konstaterat ärftlig bröstcancer.

Annars används mammografi och ultraljud + biopsi.

Utomlands händer det mycket med MRI. I Sverige är det frågan om en generationsväxling. Radiologer inom området mammografi är hittills inte lika flitiga användare av MRI.

P1, P2 & P3

På unga kvinnor skulle valet vara P3, om produkten når upp till sensitivitets- och selektivitetsnivåerna. Unga kvinnor med bröstcancer har stor risk för att dö, då har priset för kontrastmedel ingen avgörande betydelse.

För allmän screening skulle valet vara P1 på grund av priset. Det som är allra viktigast vid allmän screening är säkerheten.

För andra riskgrupper än unga kvinnor skulle valet antingen vara P2 eller P3. En fråga om nytta kontra kostnaden. Samhällsekonomisk fråga. Är det värt ett högre pris?

Appendix E – Interview with Katarina Rönnow, 2009-11-16

När används MRI idag när det gäller bröstcancer?

Okänd primärtumör vid axillmetastas. Resultat av cytostatikaterapi. Vid icke synliga tumörer på mammografi; ev. multifokalitet. För att se om misstänkt vävnad är ärrvävnad eller en ny tumör. Hereditetsstudier. Local staging preoperativt: storlek och för att undersöka det kontralaterala bröstet.

Vad tycker Ni det finns för fördelar och nackdelar med MRI?

- Hög sensitivitet (fördel).
- Låg specificitet (nackdel).

- Ganska dyr undersökning.
- Svårt att få tillräckligt med tid på de MR-maskinerna vi har.

Finns det några problem/nackdelar idag med de kontrastmedel för MRI som finns ute på marknaden?

Vi har Dotarem 4 ml/kg. VI har inte haft några bekymmer, men vi utför tyvärr bara en undersökning/vecka.

Vilka önskemål har Ni gällande nya kontrastmedel inom MRI?

Bättre specificitet. Inte så dyra. Ingen allergi.

Är det någon av dessa tre kontrastmedel som skulle göra att användandet av kontrastmedel skulle öka och i så fall varför?

Kostnaden på 20000kr för en undersökning är för mycket. Man kommer att använda sig av de andra i första hand för en ”screening” och utifrån den undersökningen gå vidare med dyrare kontrastmedel och andra undersökningar.

Appendix F – Interview with Axel Johansson, 2009-11-16

När används MRI idag när det gäller bröstcancer?

Där jag jobbar på Ängelholms Sjukhus använder vi bara MRI vid frågeställning metastaser till lever, hjärna och skelett från bröstcancer.

Vad tycker Ni det finns för fördelar och nackdelar med MRI?

- Ingen röntgenstrålning.
- När det gäller frågeställningen skelettmetastaser är fördelen att stor del av skelettet kan undersökas, tidiga metastaser som inte orsakat skelettpåverkan kan detekteras och man kan oftast skilja på metastas och degenerativa förändringar i skelettet.

- Negativt med lång undersökningstid, känsligt för rörelseartefakter, man kan inte ha pacemaker, smärtstimulatorer och liknande inopererade elektroder.

Finns det några problem/nackdelar idag med de kontrastmedel för MRI som finns ute på marknaden?

Risk för Nefrogen Systemisk Skleros samt att de är njurtoxiska.

Vilka önskemål har Ni gällande nya kontrastmedel inom MRI?

Patienterna ska tåla dessa. De ska inte vara allergena eller giftiga och de ska ge snabb effekt.

De ska vara lätta att administrera i förfyllda sprutor i rumstemperatur.

P1, P2 & P3

För populationsscreening skulle valet vara P3. Om man vet att 1 % får läggas in på sjukhus p.g.a. kontrasten för medel 1 och 2 vilket blir ca 5000 personer varje år så måste man ju ta det medlet med minst biverkningar. Screening vartannat år i 20 år av 50000 kvinnor per årsklass. Biverkningsprofilen vid screening viktig då många patienter ska utsättas för medlet.

P3 skulle även väljas för kvinnor som har 25 % eller mer ökad risk för bröstcancer. Detta eftersom en hög sensitivitet krävs.

För unga kvinnor skulle valet vara P2 då bra specificitet krävs. För kvinnor med förstagradssläktingar med bröstcancerhistorik och för kvinnor som har haft bröstcancer tidigare skulle valet vara P2, då bra sensitivitet och specificitet krävs.

För kvinnor över 70 år skulle P1 väljas. Inte så många patienter kommer ifråga och tumörerna är stora.

Är det någon av dessa tre kontrastmedel som skulle göra att användandet av kontrastmedel skulle öka och i så fall varför?

Ja, P3, eftersom biverkningsprofilen är så liten jämfört med övriga – viktigt då man undersöker friska så att man inte orsakar sjukdom genom undersökningsmetoden.