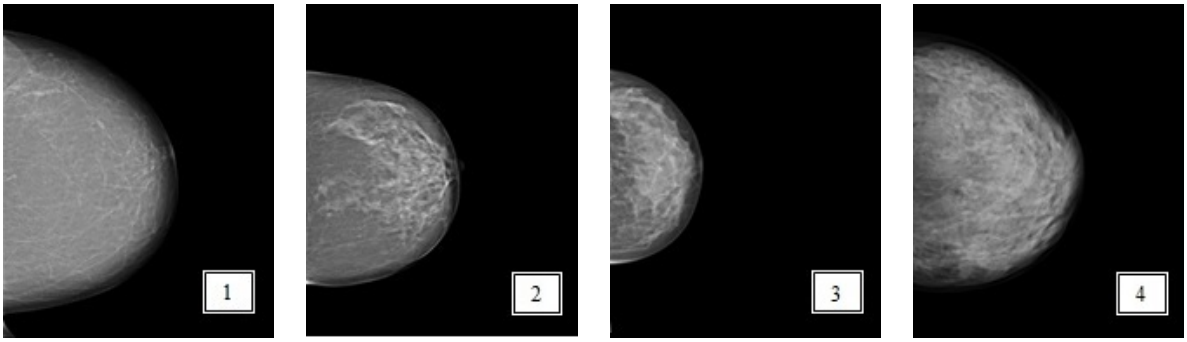
Mammography is a basic radiological examination used for diagnosing of mammary gland abnormalities. The method is based on the difference in X-ray absorption by breast tissues. This facilitates not only early detection of structural changes, such as tumors or tissue thickening, but also determination of mammographic breast density in terms of per cent content of radiologically dense tissues, i.e. tissues characterized by low X-ray radiolucency.
Photos 1-4 show four women's mammograms. The "dense" tissue is visible as bright streaks. The breast in photo 1 contains almost no glandular fibrous „dense" tissue, while in photo 4, the „dense" tissue fills almost all of the breast – the mammographic density is as high as 87%.

mammographic density (MD)

MD = 3% MD = 27% MD = 49% MD = 87%



The scientists have noted that higher mammographic density correlates with higher breast cancer risk. First epidemiological studies in this topic were initiated already in the 70s, after it had been proposed to use, in the assessment of the mammograms, the classification which included information about breast density (Wolfe, 1976). It is now generally recognized that mammographic density is an indicator/biomarker of breast cancer risk. It has been demonstrated that in women who have „dense" breasts (MD>75%), the risk is almost 5-fold higher compared to women with low mammographic density (MD<5%). Breast mammographic density decreases with age of the women and to a large degree is dependent on body mass of the woman – MD is lower in obese women as a result of more adipose tissue. It is genetically determined and higher in nulliparous women. It may probably be modified by lifestyle factors, including diet and environmental factors. Research on mammographic density and the factors that affect it have been carried out in many research centres worldwide. This research is of great importance for breast cancer prevention; it is generally recognized that the factors which affect mammographic density have direct influence on breast cancer risk. Efforts to determine breast cancer etiology continue, because in about 60% cases the cause is not determined. It is also believed that a part of breast cancer cases might result from high environmental pollution. One of the factors present in the environment which may be important in the cancer etiology, including breast cancer, is cadmium. According to American scientists, increasing exposure to cadmium may explain as many as 35% breast cancer cases in U.S. women. In Japan, where environmental exposure to cadmium is relatively high, it has been observed that in women with urine concentration of cadmium >2.62 μg/g Cr, the risk of breast cancer is up to 6-fold higher compared to the women with low cadmium exposure.
Cadmium belongs to the group of heavy metals. Examples of occupational exposure to this factor include e.g. workers of non-ferrous metal smelter works and of plants producing nickel-cadmium batteries. Environmental exposure to cadmium may, however, affect everyone because cadmium is found in food products and cigarettes. Comparison of the magnitude of exposure to cadmium performed as part of the DEMOCOPHES project during recent years in 17 European countries has demonstrated that in Poland the exposure is the highest – twice higher than the average for the total group (average concentration in urine ~0.42 μg/g Cr vs. 0.24 μg/g Cr, respectively). The likely explanation for these differences is the fact that cadmium-containing fertilizers were used in the agriculture in Poland, causing soil contamination and absorption of cadmium by plants. This metal has very long half-life in the body, up to 30 years and, after it has been absorbed by the organism, is execrated with urine at a very slow pace. Urinary cadmium concentration is a good indicator of the deposit of that metal in the human body.
The mechanisms explaining the contribution of cadmium in breast cancer initiation or progression have not been yet completely elucidated. However, it seems that the key element of the mechanism is the estrogen-like modulation of the endocrine system function. Cadmium belongs to the group of metalloestrgens and in experimental studies it has been shown that ions of cadmium are able to activate estrogen receptors. Like the female hormone estradiol, it can initiate cell division, thus affecting the structure of the mammary gland. Therefore, it seems justifiable to expect that cadmium will affect mammographic density. So far, this association has been confirmed only in one study of a relatively small group of 200 U.S. women.

The aim of our project is to assess the association between cadmium concentration in urine and mammographic density. Research hypothesis assumes that cadmium, as a metalloestrogen, affects mammographic density, and thus breast cancer risk.

The study subjects will include as many as 300 female inhabitants of Lodz, aged 40-60, not treated with hormone therapy and without breast cancer medical history or previous breast augmentation/implant surgery. Women presenting for mammography within the Screening Program for Early Breast Cancer Detection will be invited to participate in the project. Digital mammography will be performed in centers selected by the Voivodeship Centre for Coordination in Lodz.
Personal interview will be conducted with each study participant to collect information including occupational history, reproductive and lifestyle factors. We are going to measure body weight and height, hip and waist circumference and to calculate body mass index (BMI), and the indicator of abdominal obesity - waist to hip ratio. In the samples of urine to be collected, we shall determine cadmium concentration. Moreover, in blond samples, we shall measure hormone concentrations: estradiol, prolactin and the level of SHBG protein. Volpara software will be used to analyze the mammograms. Volumetric mammographic density will be calculated, that is the percentage of glandular-fibrous tissue in the total volume of the gland. Volpara software has been developed by the British/New Zealand group of researchers and is being gradually implemented by clinics in many

countries. It is the most modern tool so far, ensuring fully automated and objective method of mammogram analysis.

Our project assumes also creating a bank of biological samples, including DNA and urine samples. The DNA bank will offer potential for further research on the genetic and epigenetic factors involved in the etiology of breast cancer. The protected urine samples will enable continuation of the studies on the health effects in women and their exposure to other environmental factors, such as endocrine disruptors in connection with growing interest in their potential adverse effects in terms of hormone-dependent pathologies.

Potential practical importance of the project stems from the application of diagnostic mammography improved as the result of implementation of higher standards for the analysis of mammographic images, including quantitative assessment of mammographic density.