BISPHOSPHONATE-FUNCTIONALIZED GOLD NANOPARTICLES AS A TARGETED X-RAY CONTRAST AGENT FOR BREAST MICROCALCIFICATIONS

Abstract

by

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Breast cancer is the most common cancer and the second leading cause of cancer-related deaths among women. Early detection is considered the best option for reducing morbidity and mammography is the current gold standard for early detection of breast cancer. Microcalcifications are the most common abnormality observed on a mammogram and are early markers for breast cancer. However, the detection of breast microcalcifications and correct diagnosis of breast cancer are limited by the sensitivity and specificity of mammography, especially in women with radiographically dense breasts. Mammography could potentially be improved by the administration of a contrast agent for contrast-enhanced X-ray imaging. Therefore, the objective of this research was to investigate the potential of bisphosphonate-functionalized gold nanoparticles (BP-Au NPs) as an X-ray contrast agent for targeted labeling and contrast-enhanced radiographic imaging of breast microcalcifications. The hypothesis was that BP-Au NPs would target and enhance the X-ray contrast of microcalcifications enabling improved sensitivity and specificity for X-ray detection of microcalcifications. *In vitro*, *ex vivo* and two *in vivo*

models of microcalcifications were developed and used to investigate BP-Au NPs. BP-Au NPs provided enhanced-contrast for the detection of microcalcifications in each model, including a model of radiographically dense mammary tissues. BP-Au NPs targeted microcalcifications *in vivo* after intramammary delivery to enhance X-ray contrast with surrounding mammary tissue, which resulted in improved sensitivity and specificity. In summary, the utility of using BP-Au NPs as a targeted X-ray contrast agent was demonstrated, suggesting that BP-Au NPs could provide a more sensitive and specific diagnostic tool for the detection of microcalcifications during mammographic screening for breast cancer.