The role of connexin-mediated intercellular communication in radiation-induced atherosclerosis

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PhD Highlights

There are currently no radioprotective treatments available that have clinically been approved to be effective against potential atherosclerotic complications after breast cancer radiotherapy.

- We here provide novel insights into the molecular mechanisms of radiation-induced vascular endothelial damage, and identified connexin43 hemichannels as a potential therapeutic target to suppress certain early atherosclerosis markers induced by radiation (Patent filed).

- We identified two potential biomarkers, GDF-15 and CXCL10, that could be considered after validation studies for early detection of atherosclerosis risk in radiotherapy-treated breast cancer patients, thus identifying patients who may benefit from early medical intervention.

Ultimately, the results of this PhD will help in improving the risk assessment of atherosclerosis and would help in reducing the atherosclerosis burden in breast cancer radiotherapy patients.

Curriculum Vitae

Oct 2015- Sep 2019 Ph.D. student, Faculty of Medicine and Health Sciences, Physiology group, Department of Basic and Applied Medical Sciences, Ghent University, Belgium & Radiobiology Unit, SCK•CEN, Belgium

Sep 2013- Jul 2015 Master of Biomedical Science, Hasselt University, Hasselt, Belgium

Jan 2010-Jul 2013 Scientific Researcher, Biomedical Informatics & Chemoinformatics, National Research Center, Egypt

Sep 2004- Jul 2009 Bachelor of Pharmacy and Biotechnology, German University, Egypt

Selected Bibliography:


Radiotherapy is an effective treatment for breast cancer and other thoracic malignancies. However, while radiotherapy successfully kills cancer cells, unavoidable radiation exposure to the heart and large arteries occurs during treatment, resulting in radiation-induced heart disease, especially atherosclerosis. Atherosclerosis is initiated by damage to endothelial cells that line the blood vessels. Endothelial cells express connexin (Cx) proteins that are reported to exert proatherogenic as well as atheroprotective effects. Furthermore, Cxs form channels, gap junctions and hemichannels, that are involved in intercellular communication between the endothelial cells and surrounding cells.

The aim of this PhD was to investigate the role of Cxs and their channels in radiation-induced atherosclerosis, for the aim of better risk assessment and therefore better radiation protection after thoracic radiotherapy.

We demonstrate that radiation exposure increases pro-atherogenic Cx43 levels and decreases atheroprotective Cx40 levels, potentially contributing to atherosclerosis development. In addition, radiation exposure enhances intercellular communication between endothelial cells by increasing gap junctional communication and inducing Cx43 hemichannel opening. Together, these effects promote the spread of radiation-damaging signalling thereby exacerbating endothelial cell damage and initiating atherosclerosis development.

Moreover, we show that inhibiting Cx43 hemichannels without inhibiting gap junctions protects irradiated endothelial cells against oxidative stress, cell death, chronic inflammation and premature cell senescence. These markers are known to contribute to endothelial dysfunction, an early marker for atherosclerosis. Therefore, targeting Cx43 hemichannels may help in the establishment of novel therapeutic strategies to mitigate atherosclerosis in thoracic radiotherapy treated patients.

**Summary**

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