P37 Simultaneous detection of the cancer biomarkers zinc and citrate in prostate cancer tissue using mass spectrometry imaging

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Andersen M.K.[1], Krossa S.[1], Høiem T.S.[1], Bucholz R.[2], Claes B.S.R.[3], Balluff B.[3], Ellis S.[3], Richardsen E.[4], Bertillsson H.[5], Heeren R.M.A.[3], Bathen T.F.[1], Karst U.[2], Giskeødegård G.F.[1], Tessem M.[1]

[1]Norwegian University of Science and Technology, Department of Circulation and Medical Imaging, Trondheim, Norway, [2]University of Münster, Institute of Inorganic and Analytical Chemistry, Münster, Germany, [3]Maastricht University, Maastricht MultiModal Molecular Imaging Institute (M4I), Maastricht, The Netherlands, [4]The Artic University of Norway (UiT), Department of Medical Biology, Tromsø, Norway, [5]Norwegian University of Science and Technology, Department of Clinical and Molecular Medicine, Trondheim, Norway

Introduction & Objectives: Healthy prostatic epithelial tissue contains high levels of the metabolite citrate and the metal zinc. It is proposed that zinc causes accumulation of citrate by inhibiting further utilization through the citric acid cycle. During prostate cancer (PCa) progression, reduced levels of both citrate and zinc are reported and are therefore proposed as clinical biomarkers of aggressiveness. In this study, we detected citrate and zinc in PCa tissue simultaneously, using matrix assisted laser desorption/ionization time-of-flight mass spectrometry imaging (MALDI-TOF MSI).

Materials & Methods: A total of 45 PCa tissue sections (15 patients) were measured with MALDI-TOF MSI in negative ion mode at 30µm spatial resolution. The same tissue sections were stained with H&E and annotated by an experienced uropathologist. All acquired spectra were grouped according to tissue type; non-cancer epithelium, stroma or cancer. Zinc in the form of $ZnCl_3^-$ was identified through inspection of the isotopic peak pattern consisting of a total of nine masses (range *m/z* 168.83 - 178.82) and by accurate mass (MALDI-Orbitrap). To further confirm the presence of zinc, an adjacent tissue section was analyzed for total zinc with laser ablation inductivity coupled plasma (LA-ICP) MSI. Citrate (*m/z* 191.02) was identified through tandem MS. The relative intensities of $ZnCl_3^-$ (*m/z* 172.83) and citrate across tissue types were analyzed through linear mixed models (LMM) and Pearson statistics.

Results: Total LA-ICP MSI zinc detection showed a similar spatial distribution to $ZnCl_3^-$ measured with MALDI-TOF MSI, confirming the reliability of MALDI to detect zinc. Citrate and zinc were significantly correlated with each other ($r=0.64$, $p<0.001$, see figure),and both had reduced levels in cancer and stroma compared to non-cancer epithelium (LMM, $p<0.05$).

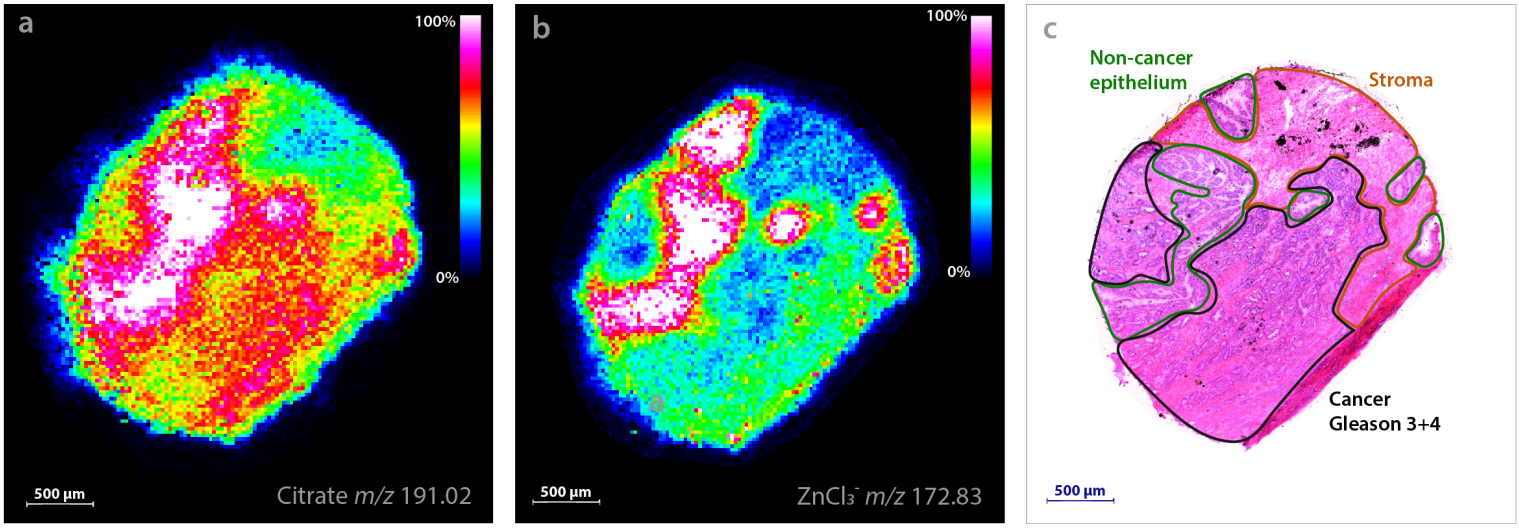

Figure: Spatial distribution of a) Citrate and b) $ZnCl_3^-$ measured with MALDI-TOF MSI, and c) H&E staining of the same tissue section.

Conclusions: We were for the first time able to detect the spatial distribution of citrate together with zinc in the same exact measurement on PCa tissues. Since lower levels of citrate in cancer epithelial tissue is associated with more aggressive PCa, the regulation of zinc may play an important role in PCa progression. Simultaneous spatial detection of citrate and zinc with MALDI-TOF MSI may be a promising tool both for PCa diagnosis and prognosis.