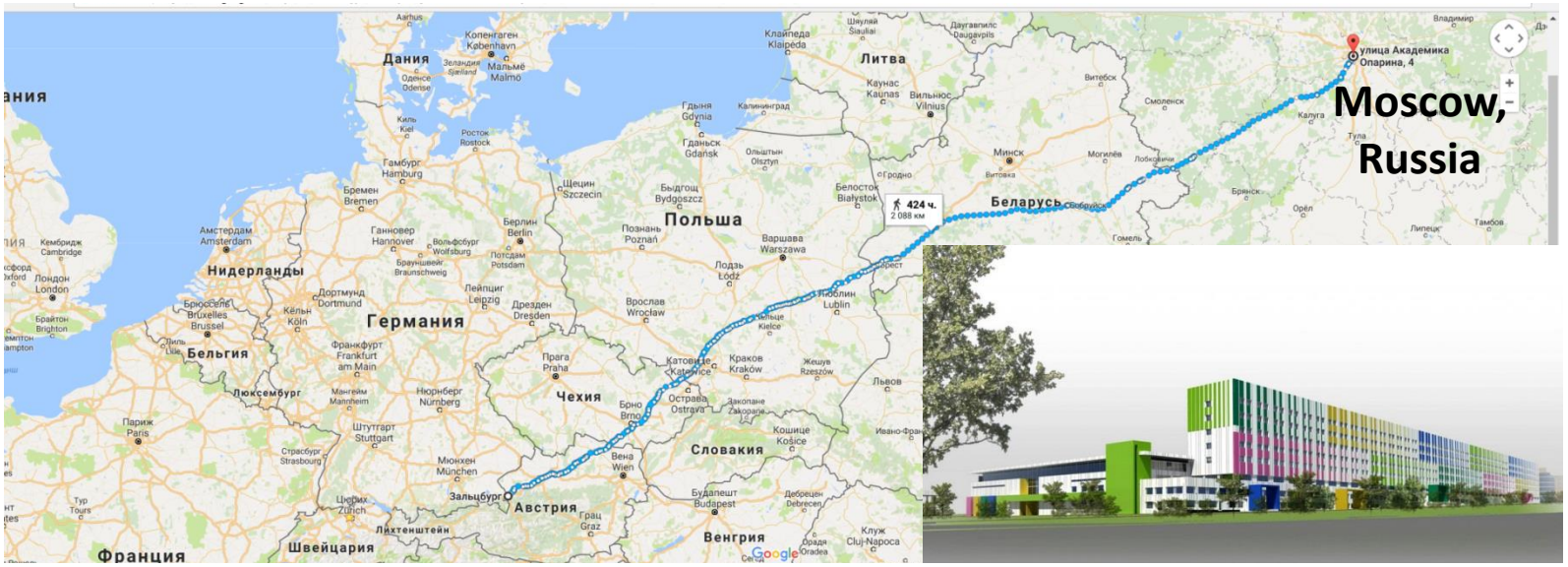


National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I.Kulakov of Ministry of Healthcare of Russian Federation

Chemical Scanning of Cancer Tissues by the Combination of Mass Spectrometry with Molecular Resonance Probe Desorption

Vladimir Frankevich, Vitaliy Chagovets, Alisa Tokareva, Alexey Kononikhin, and Gennady Sukhikh.

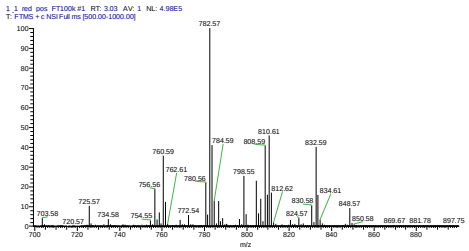
Biological Sample Analysis by Mass-Spectrometry

Gas-Phase Samples (Breath)

Liquid Samples (Blood, Urine, etc.)

Solid Samples (Tissues)

Sample Preparation or Direct MS



MS Analysis

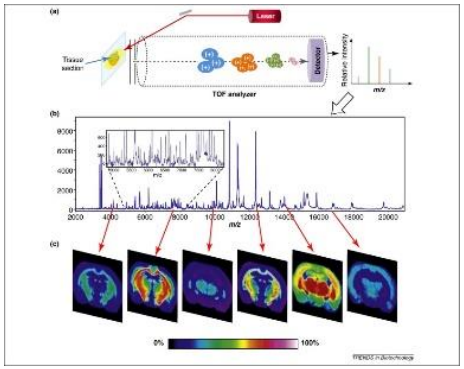
Sample Molecular Composition or Molecular Profiling

Data Base

Sample or Pathology Identification

Off-line Methods for Tissue Analysis

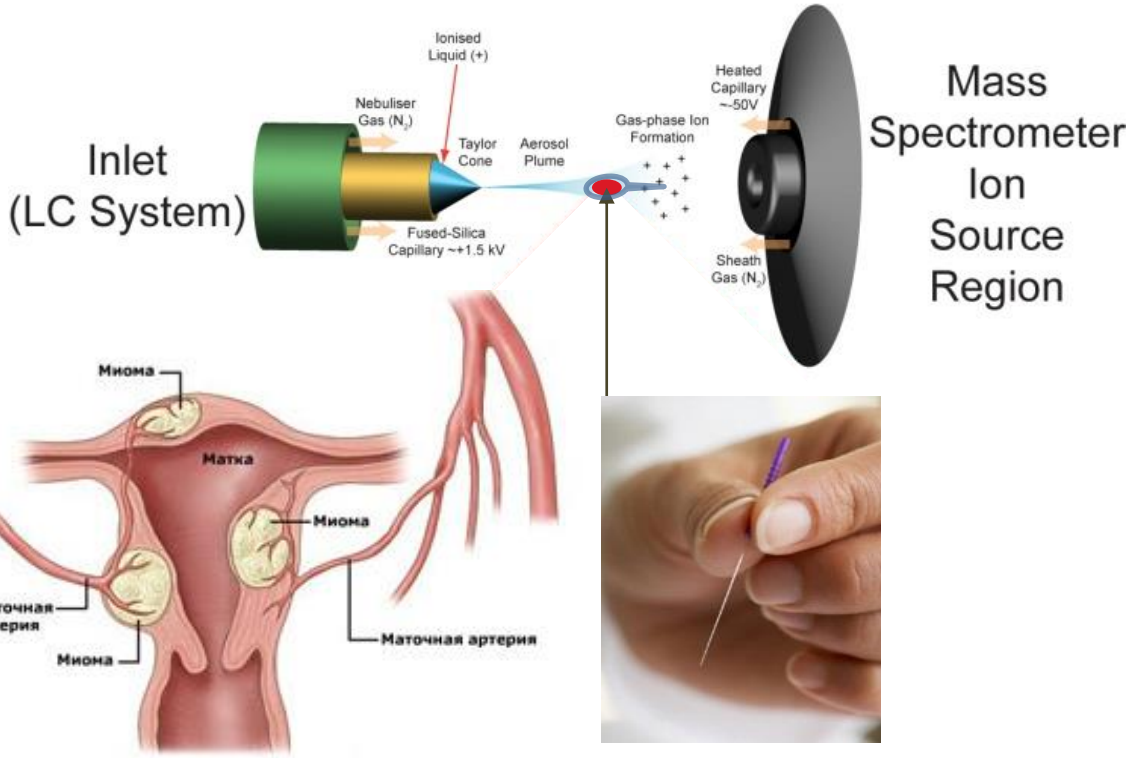
Sample extraction and LC-MS

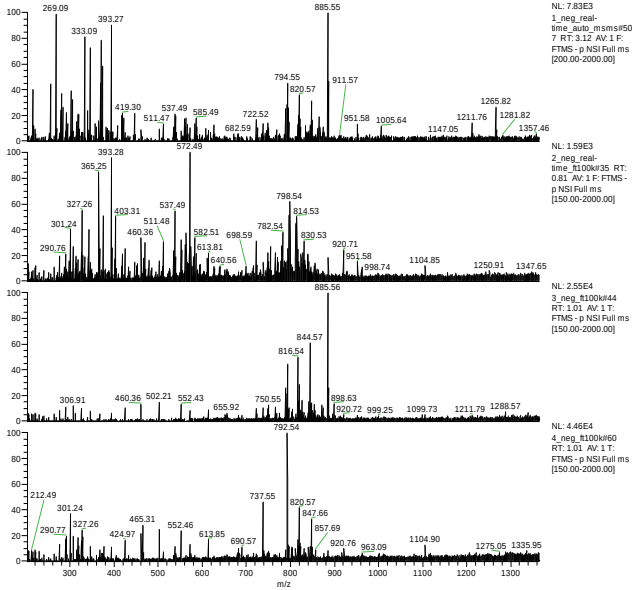


MALDI imaging

Ambient MS

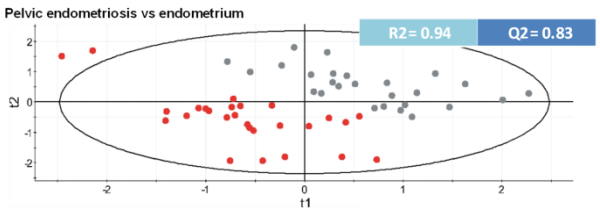
Spray from Needle



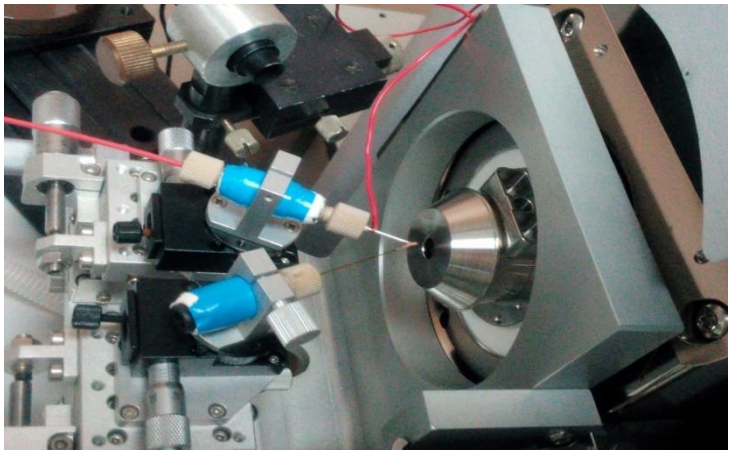


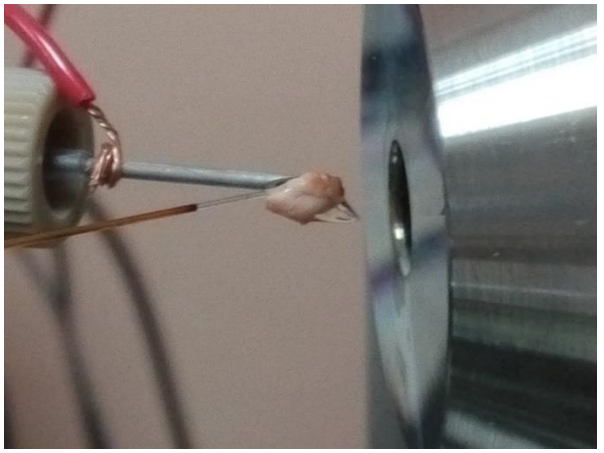
PLS-DA scores plots

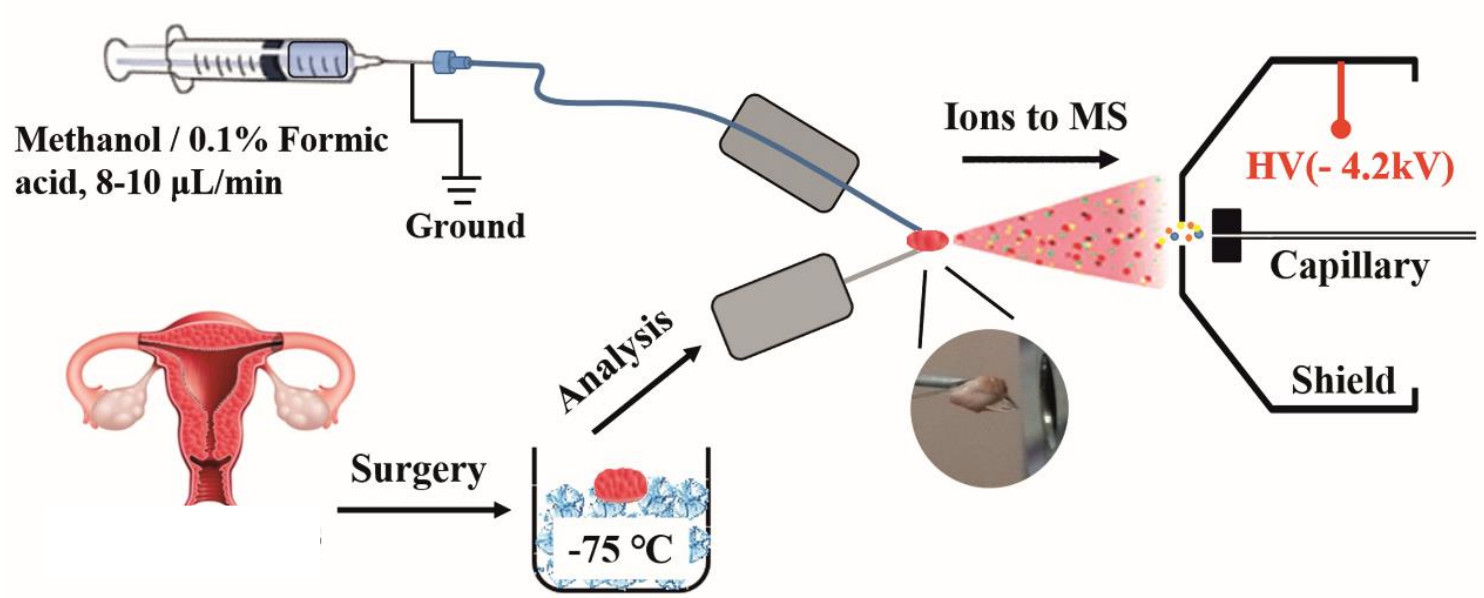
Essential differences of endometrioid tissue from endometrium



Tissue Spray







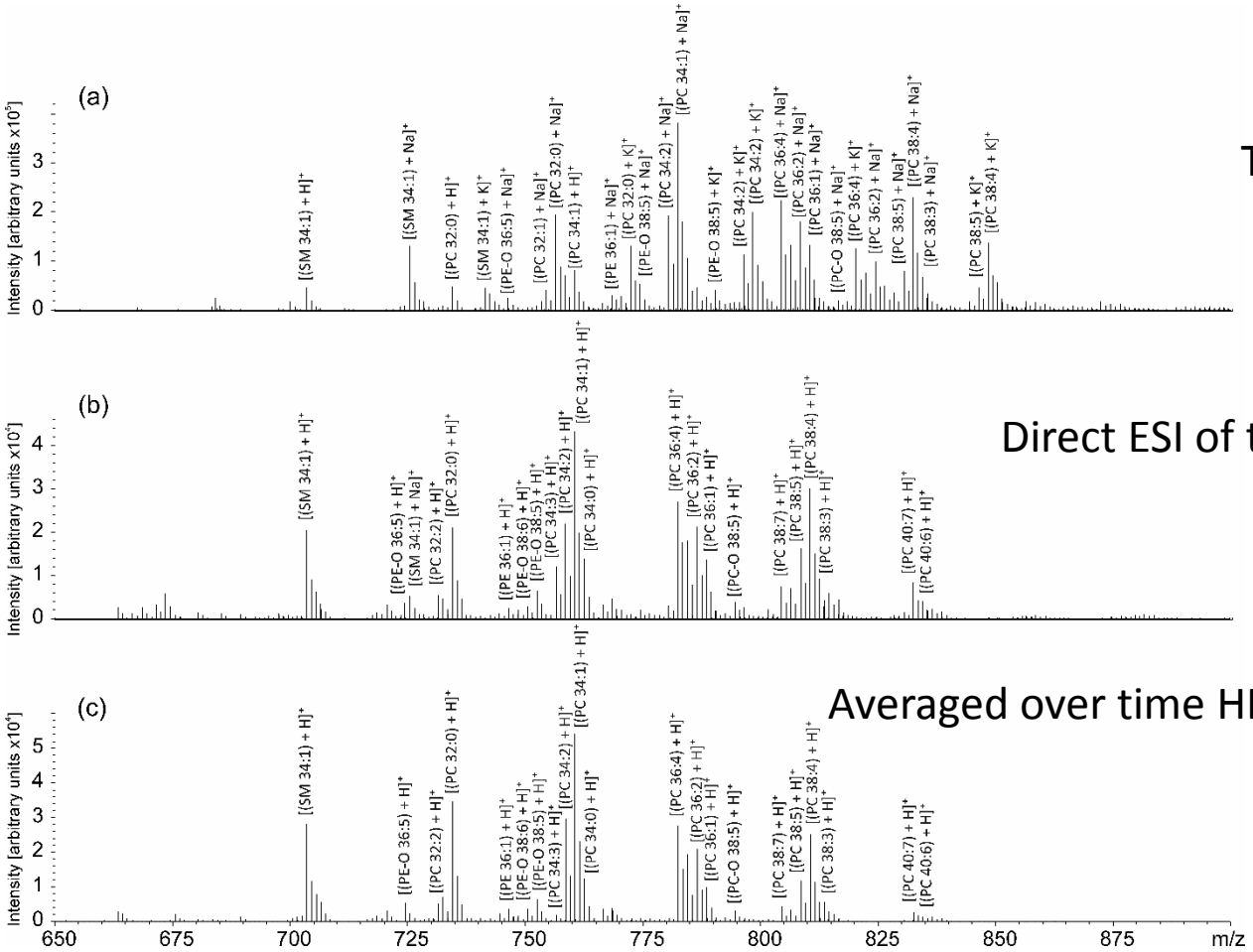
A comparison of direct tissue spray ionization mass spectrometry and offline electrospray ionization mass spectrometry of lipid extracts for the differentiation of endometrial tissues by localization

Ambient mass spectrometry and Direct Tissue Spray in particular, enables the analysis of complex samples under atmospheric pressure without or with minimal sample pretreatment.

This allows fast screening of molecular composition which is essential for high-throughput analyses in biomarkers search, development of tissue pathologies classification based on molecular composition including cancer staging and progress in personalized medicine

The present work addresses the comparison of tissue spray MS , lipid extract ESI-MS and LC-MS for the differentiation between endometriotic tissues of different foci

A comparison of direct tissue spray ionization mass spectrometry and offline electrospray ionization mass spectrometry of lipid extracts for the differentiation of endometrial tissues by localization



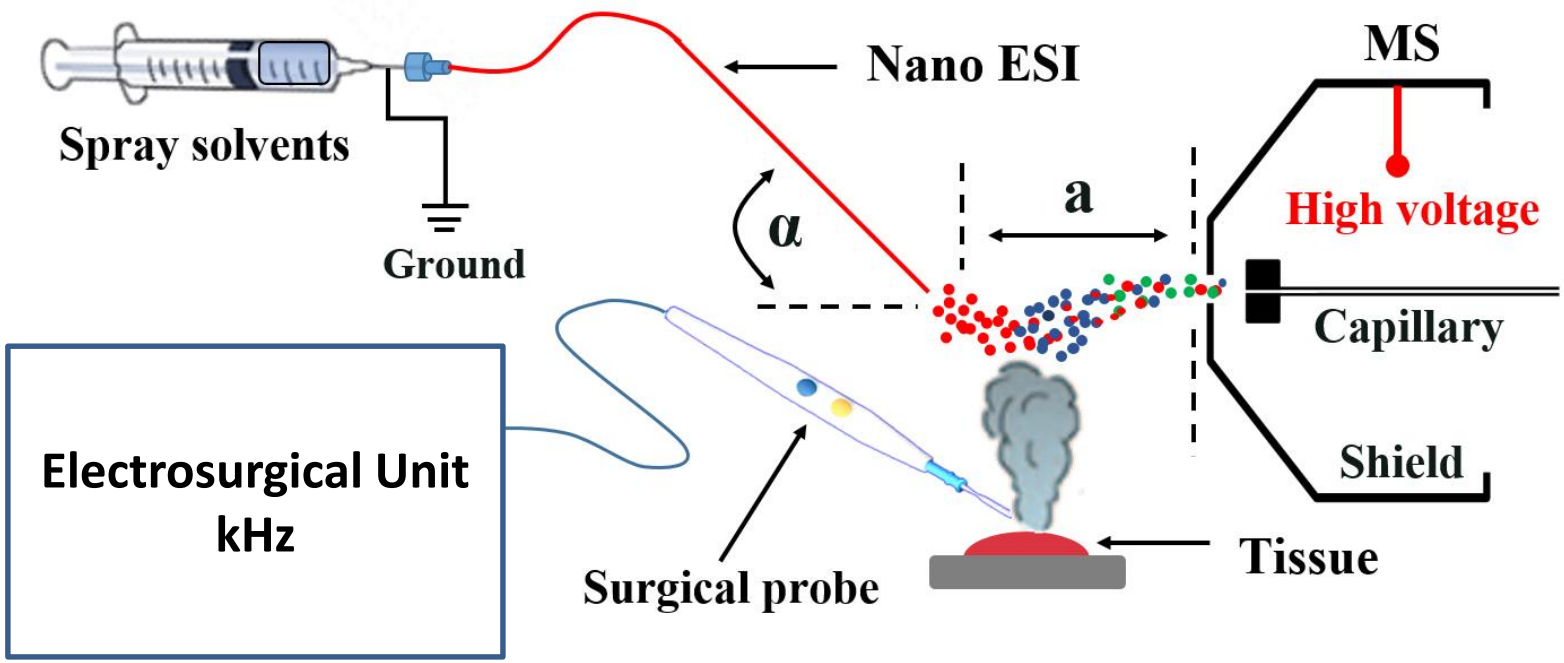
Tissue spray spectrum

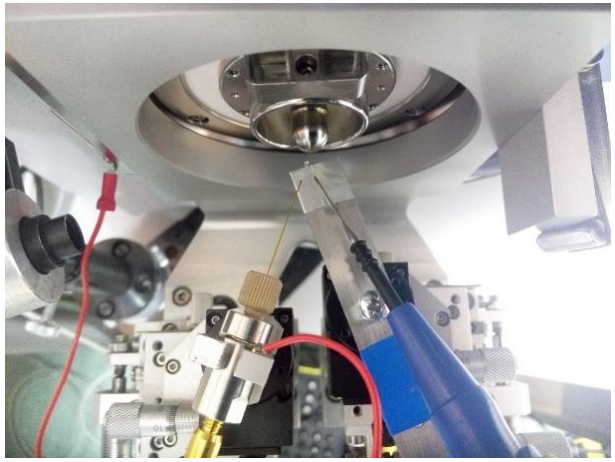
Direct ESI of the tissue lipid extract

Averaged over time HILIC/MS mass spectrum

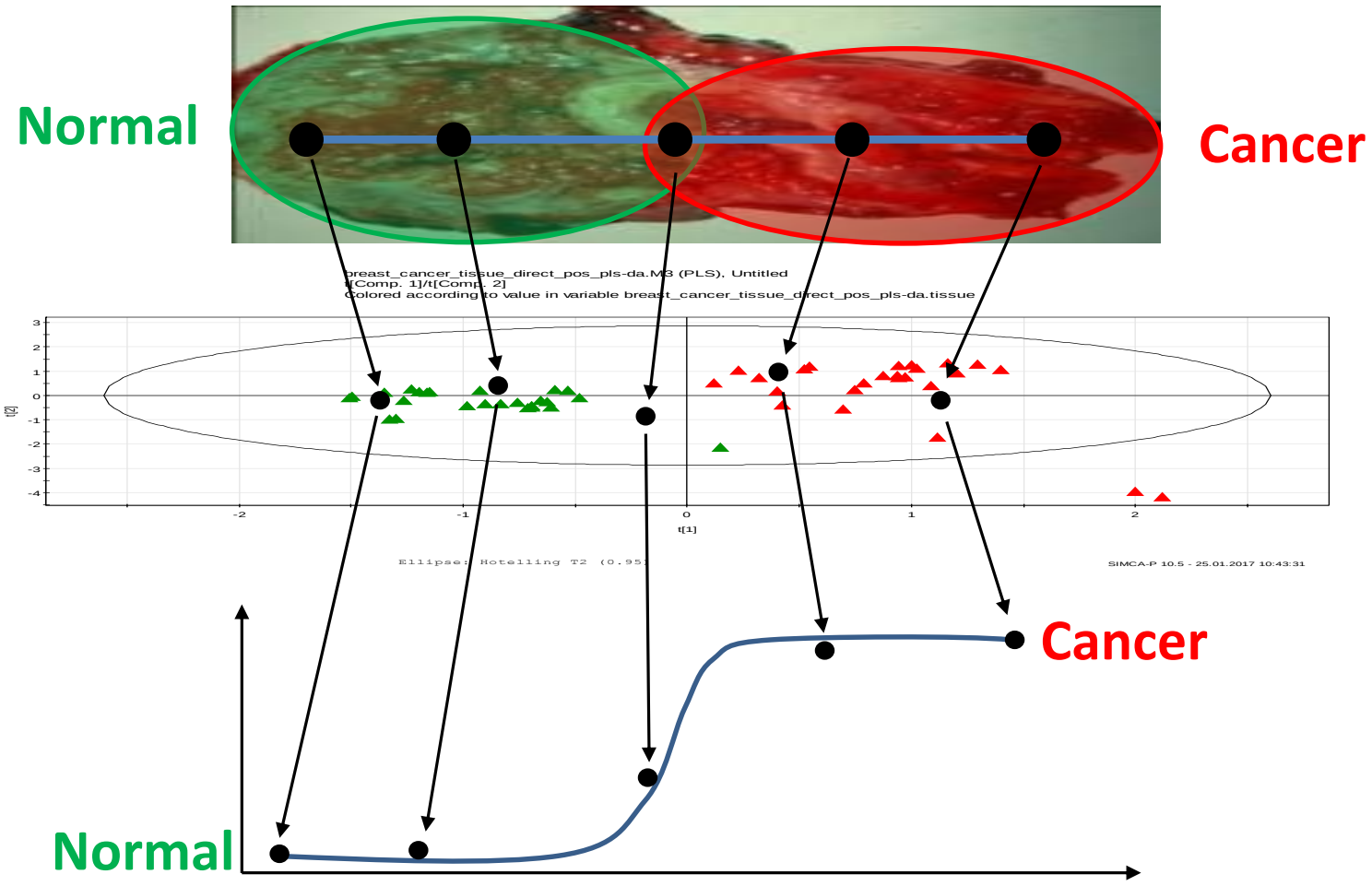
JASMS, 2017, in print

Direct Tissue MS Analysis with Surgical Probe

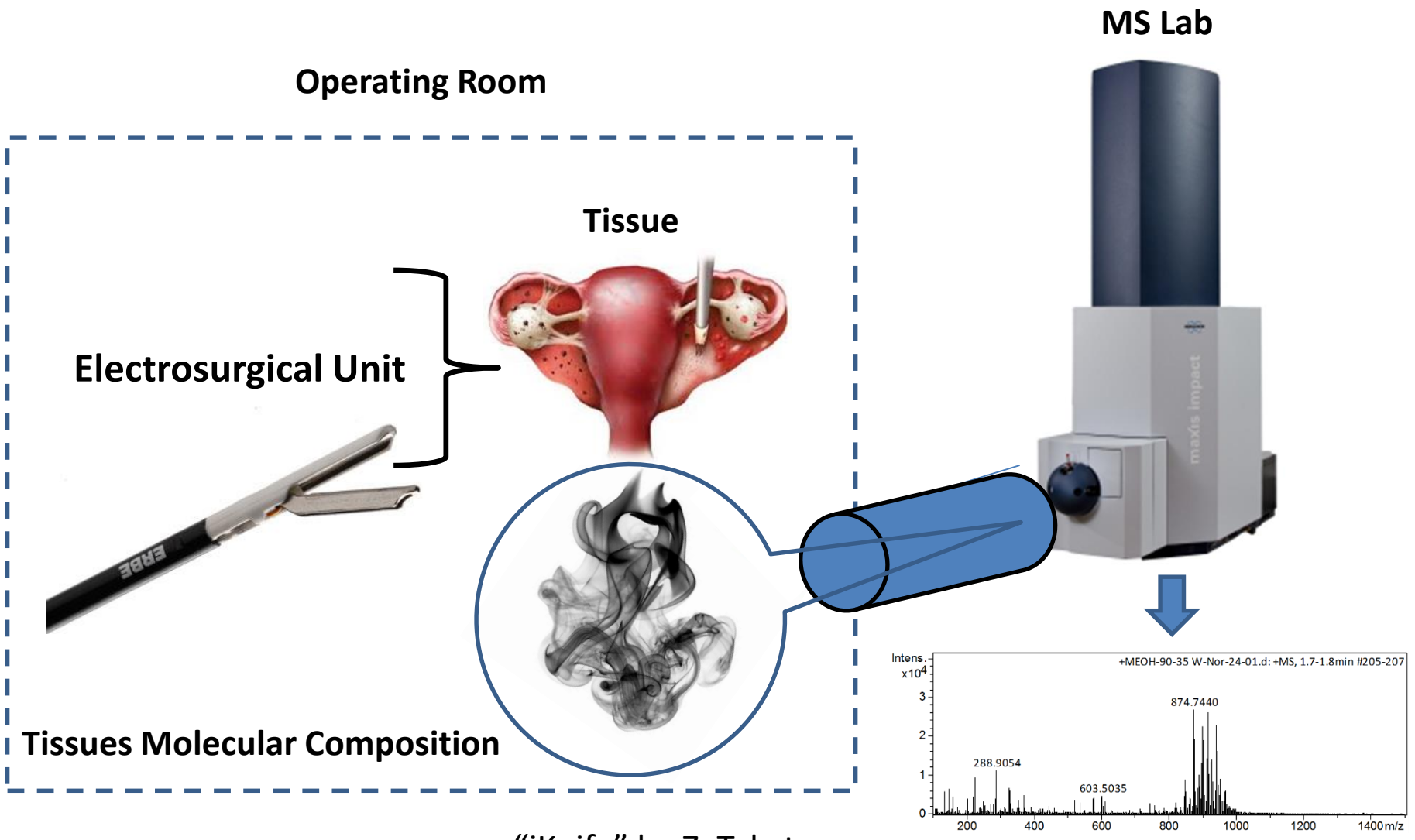




Cancer Margin



On-line Tissue Analysis

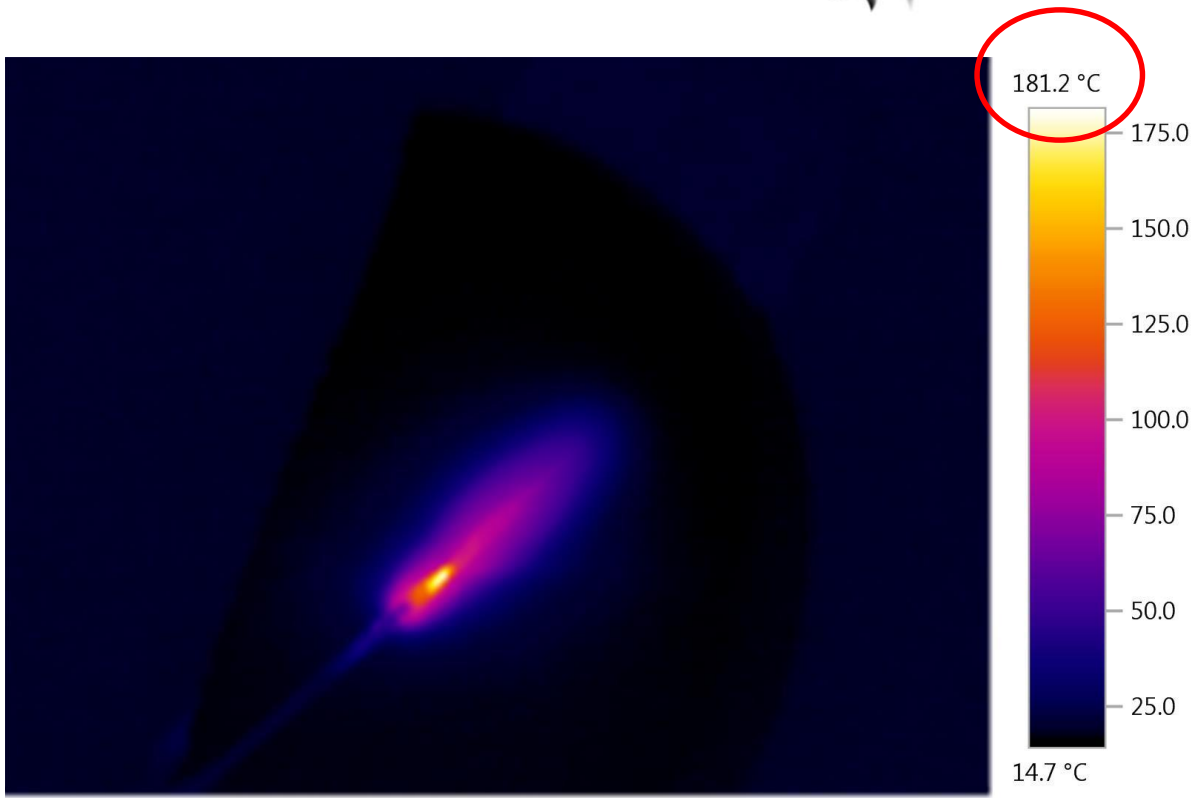


"iKnife" by Z. Takats

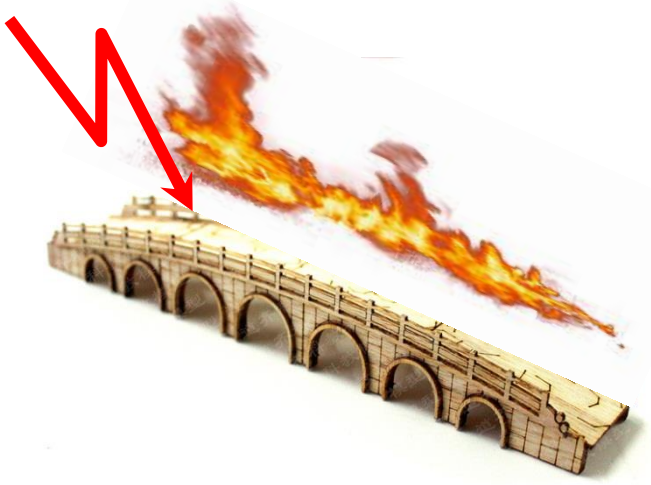
On-line Tissue Analysis

Electrosurgical unit (kHz)

?



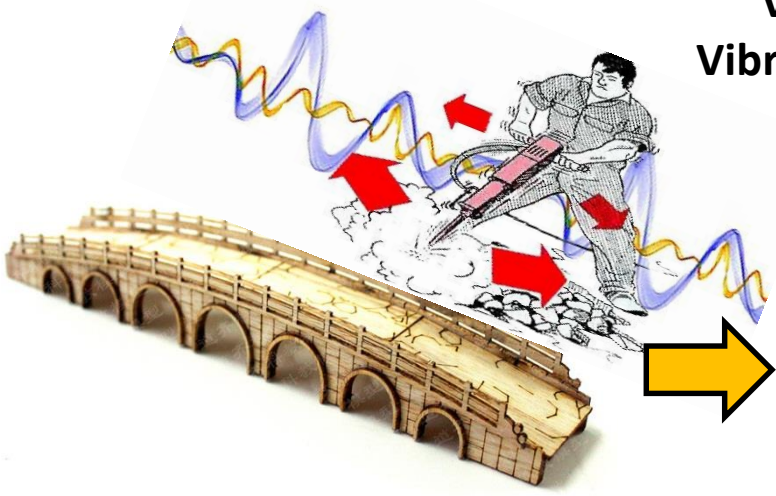
Non destructive tissue analysis



wood combustion

MC analysis

?



Vibration destruction:
Vibration on own frequency

Quantum Molecular Resonance

Quantum Molecular Resonance (QMR) technology was recently developed as a surgical tool for tissue dissection [1]. In QMR a well-defined spectrum of high-frequency electromagnetic field is produced to selectively break molecular bonds without inducing a significant rise in local temperature. Here we demonstrate QMR technology as a novel desorption source for mass-spectrometry (QMRD). Extractive Electrospray Ionization (EESI) [2] technique was used for ionization. We show that the combination (QMRD-EESI) allows on-line ambient molecular analysis of biological tissues with high chemical sensitivity.

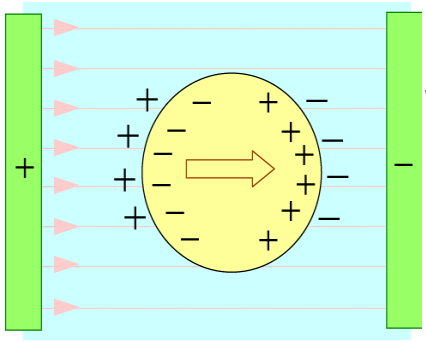
MHz range

1.Pozzato G., Vignato G.: Teoria della risonanza quantica molecolare nella realizzazione del bisturi elettronico 'Vesalius'. Quintessence Int., 2003: 5/6, p. 153–155.

2.Chen, H.W., A. Venter A., and Cooks R. G.: Extractive electrospray ionization for direct analysis of undiluted urine, milk and other complex mixtures without sample preparation. Chemical Communications, 2006(19): p. 2042-2044.

Quantum Molecular Resonance Theory

Maxwell-Wagner polarization



Wagner, K.W. Archiv f. :
Erklärung der dielektrischen Nachwirkungsvorgänge auf Grund Maxwellscher Vorstellungen.
Elektrotechnik : 1914; 371(2).

Formation intermolecular bonds by the effect incytoplasm, the plasma membrane and the surrounding extracellular medium

Foster K. R., Schwan H. P. : Dielectric properties of tissues and biological materials: a critical review.
Critical reviews in biomedical engineering 1989;17(1):25-104.

F.Kremer , A. Schonhals:
Broadband Dielectric Spectroscopy
DOI: 10.1007/978-3-642-56120-7
ISBN: 978-3-642-56120-7

oscillation frequency of the bonds in mammalian cells ≈4 MHz

Kürschner M., Nielsen K., Andersen Chr.:
Interaction of Lipophilic Ions with the Plasma Membrane of Mammalian Cells Studied by Electrorotation.
Biophysical Journal: 1998; 74(6):3031-3043
DOI: 10.1016/S0006-3495(98)78011-7

Quantum Molecular Resonance Desorption and EESI ionization

QMR probe

Tissue

SAMPLE

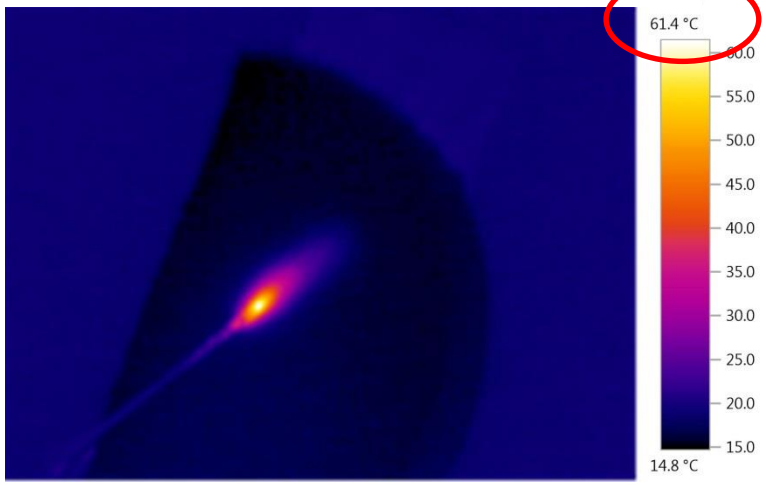
MS

Sampling cone

Ionizing spray

Solvent

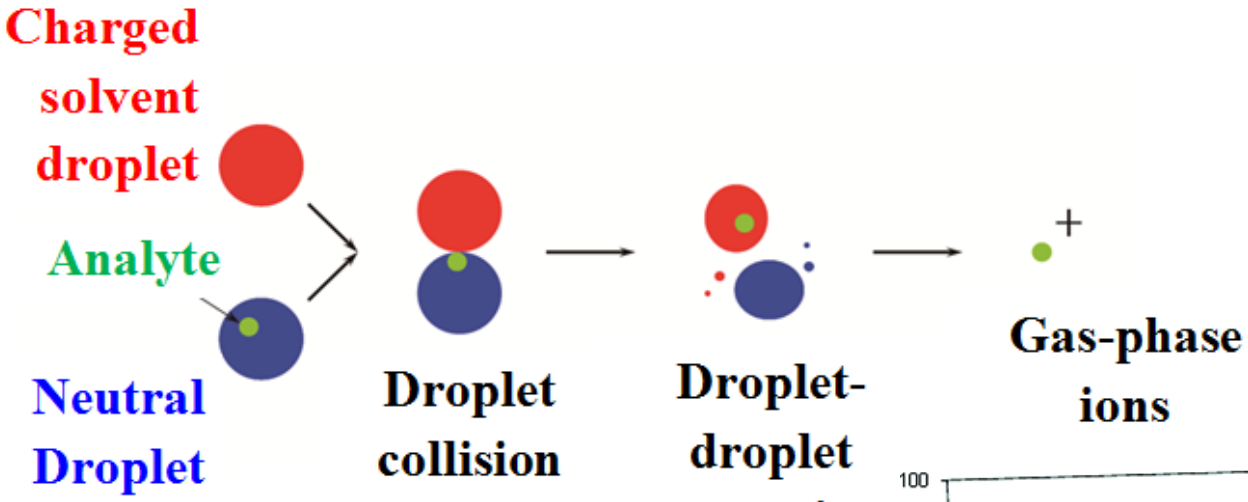
EESI

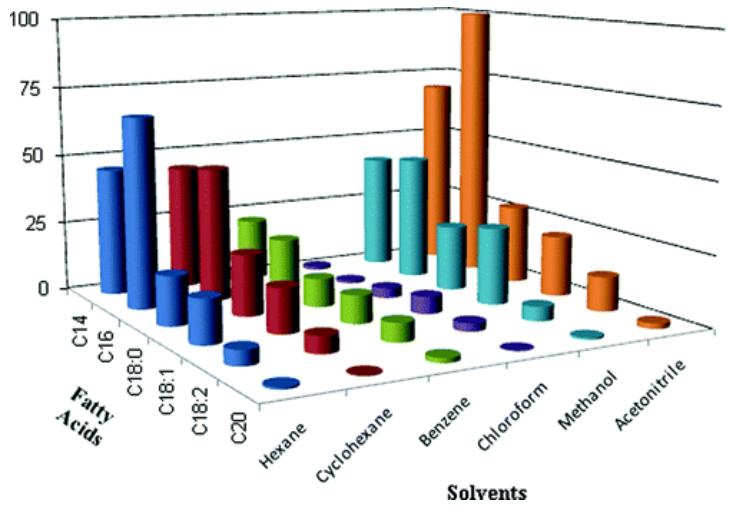


UNIQUE MASS SPECTRUM!

Advantages of EESI

Chemical composition of ionizing solution determines the efficiency of extraction and ionization process





New dimension to increase the chemical specificity of ionization

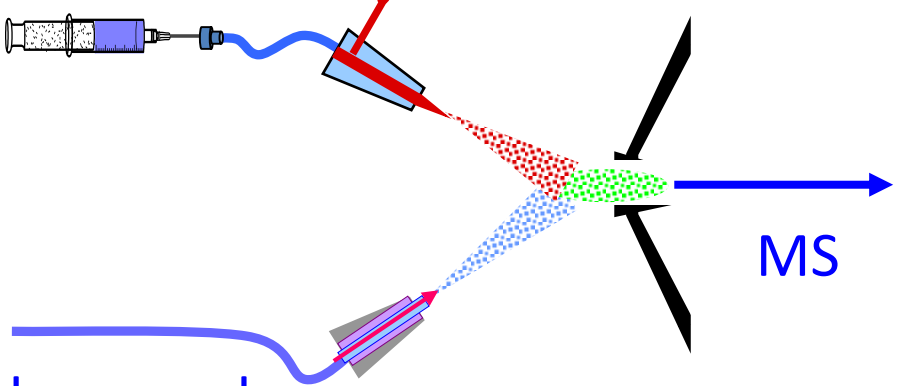
Advantages of EESI

EESI for "in-droplet" chromatography

Solvent gradient

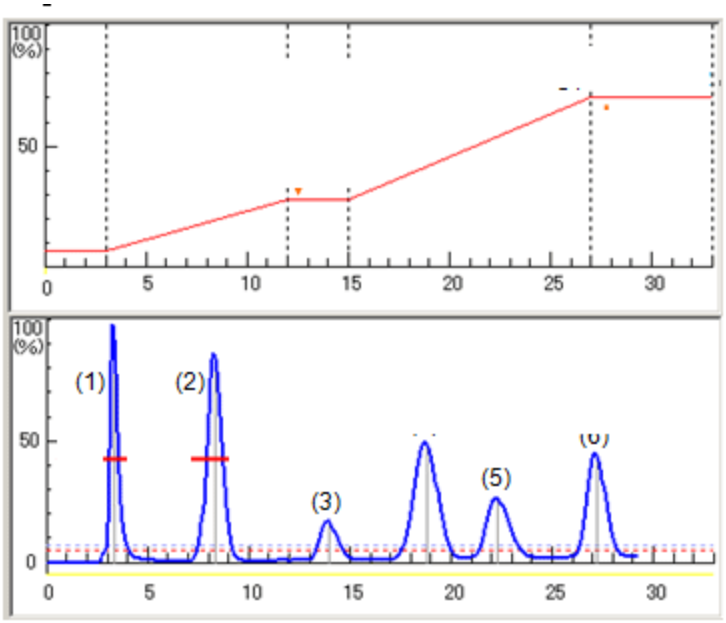
Ionizing solution

HV



MS

Complex sample solution from tissue

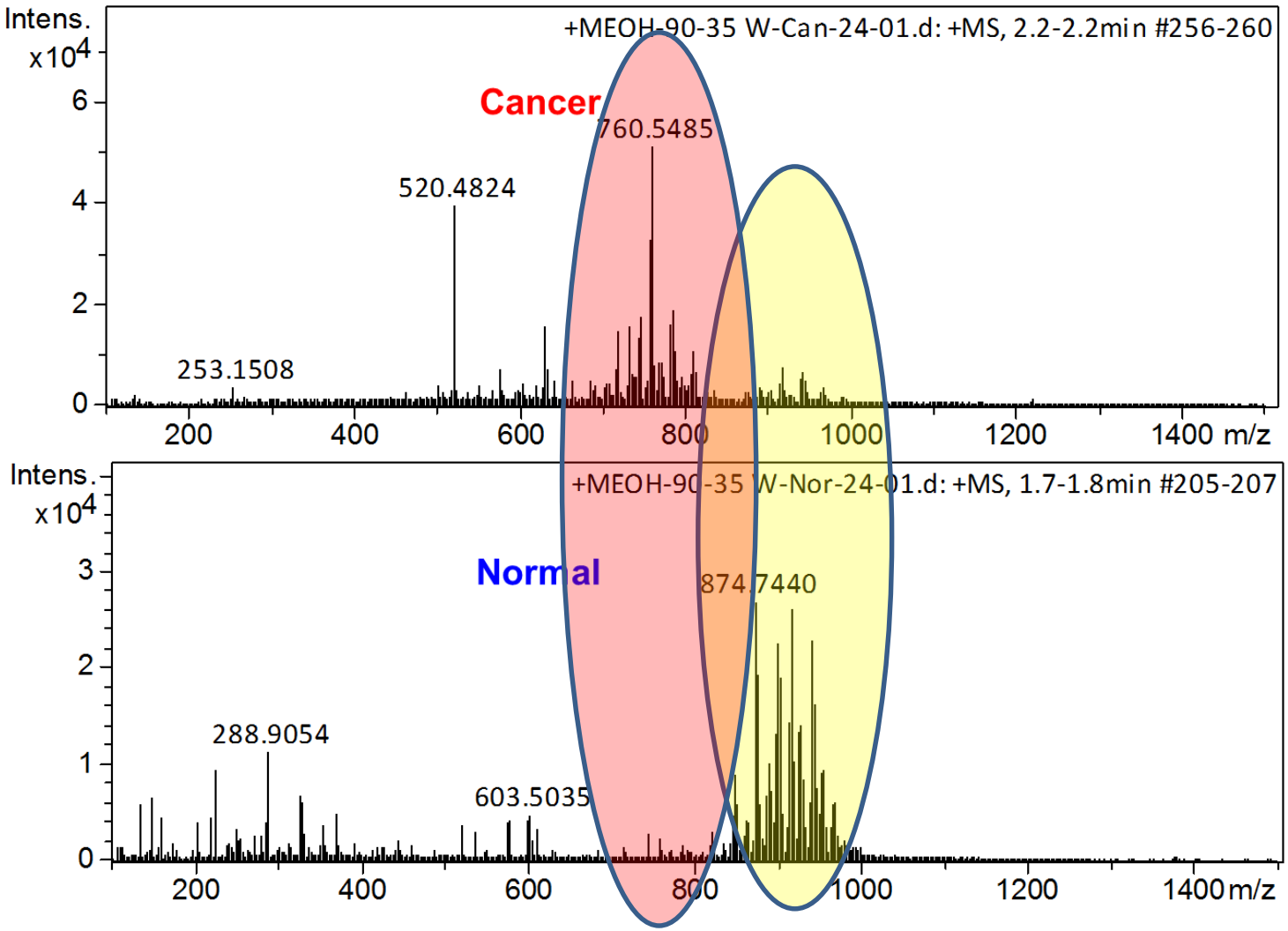


Time, s

No column

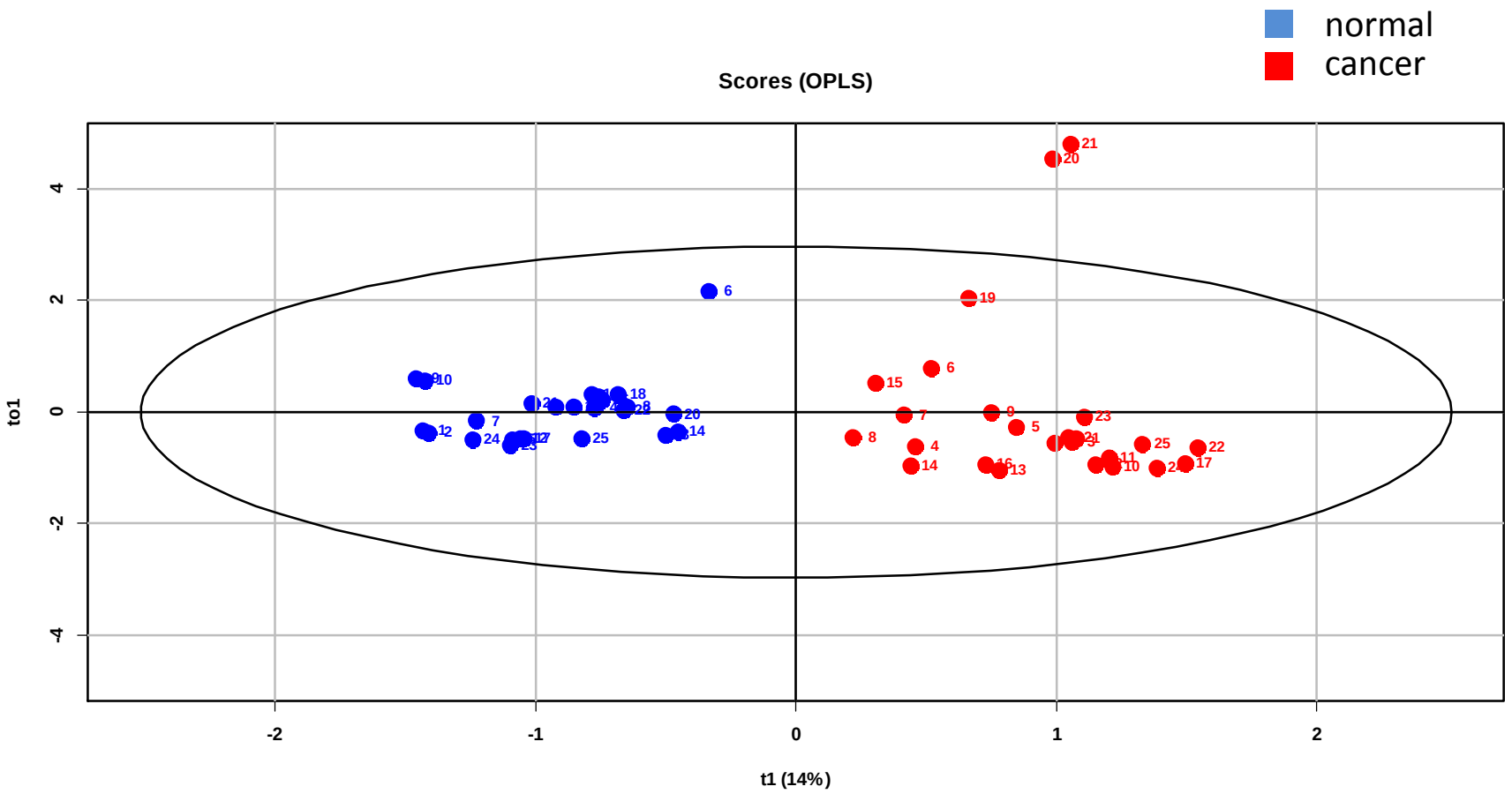
Gradient can be finished within seconds

Breast Cancer Tissues Analysis by QMRD-EESI

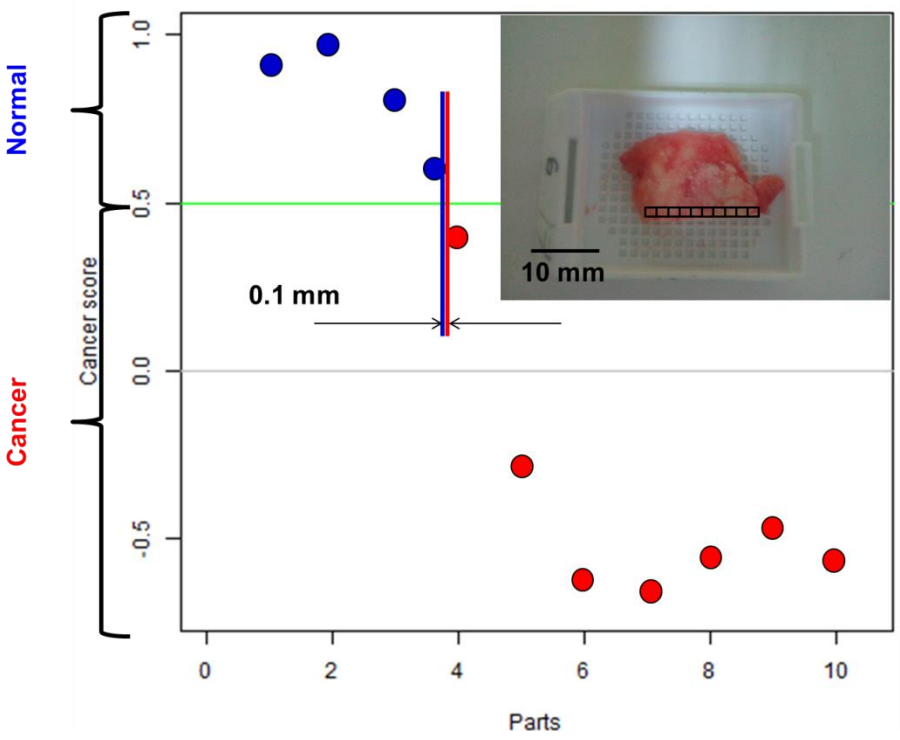


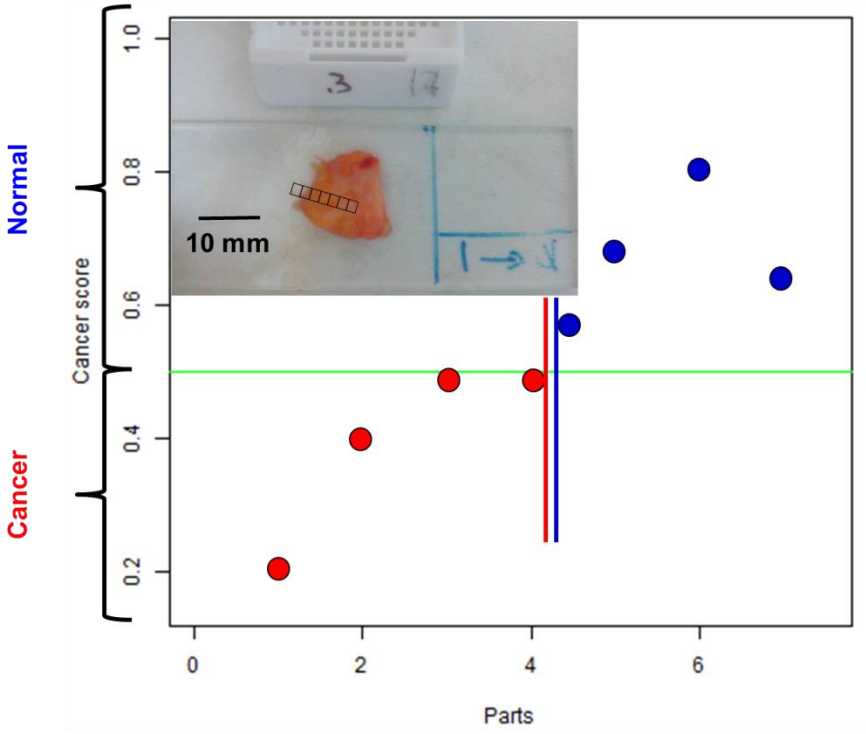
Anal. Chem. 2017, under revision

Breast Cancer Analysis by QMRD-EESI: OPLS-DA

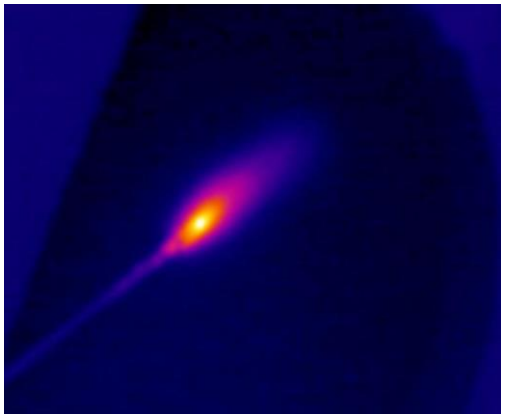


Breast Cancer Margin Determination by QMRD-EESI





High



Low

Conclusions

QMRD-EESI could be a good addition to the number of other beautiful techniques for intraoperative tissue identification

Acknowledgments

This work was supported by Russian Science Foundation grant (agreement No. 16-14-00029).

Thank you for your attention!