BioTarget - Ionizing Radiations Effects on Biological Targets

The project started in September 2017; it will be run until August 2018

Coordinator: **Simonetta Croci** - Professore Associato
Dipartimento di Medicina e Chirurgia, Unità di Neuroscienze, Università di Parma

Participants:

- **Luca Bruni**: **grant Centro Fermi** September 2017 – 31th August 2018
- **Massimo Manghi** – Dip. Medicina e Chirurgia, Università di Parma – Ricercatore
- **Walter Tinganelli** – TIFPA – Trento – Ricercatore

Rome, 9 March 2018

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BioTarget - Ionizing Radiations Effects on Biological Targets

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Work placecs & Collaborations:

- **Dipartimento di Medicina e Chirurgia, Unità di Neuroscienze, Università di Parma**
- **CIM** – Centro Interdipartimentale Misure – Università di Parma
- **TIFPA** - Trento Institute for Fundamental Physics and Applications.
- **CENTRO DI PROTONTERAPIA** - Trento

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PROJECT GOAL 2017 – 2018: the investigation of cell cytoskeleton and plasmatic membrane as biological targets of ionizing radiations.

- **Protocol setting of proton and X-ray irradiation of Hs 578Bst cell line.**
- **Cell membrane denaturation, followed by cell fixation.**
- **Atomic Force Microscopy measurements** (cell topographies)**.**
- **Computational analysis of the AFM images.**
  (M. Manghi *et al*: MDI: integrity index of cytoskeletal fibers observed by AFM. EPJPlus - 2016)

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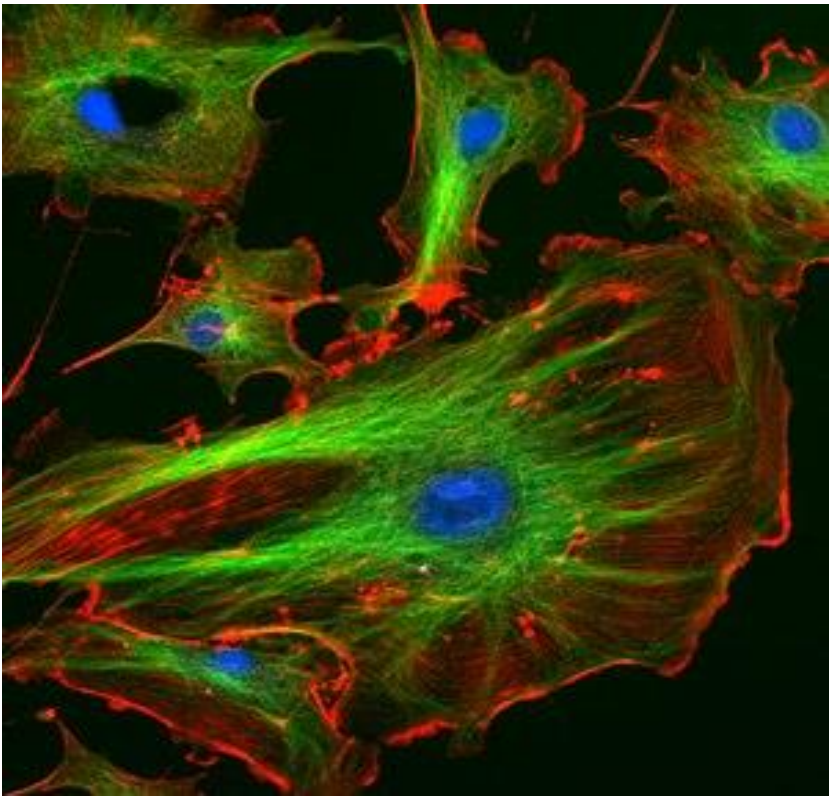
TARGETS



Microtubules

Tubuline – diam 25 nm

Cell movement

Cell shape

Track for organelle movements

Spindle for mitosis and meiosis

Microfilaments

Actin – diameter 4-7nm

Cell movement

Cell shape

Organelle movements

Muscle cell contraction

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Proton cell irradiation setting

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Proton cell irradiation setting

PROTON THERAPY CENTER - Trento

Hs 578Bst cell line irradiated with **protons**. Doses: 2Gy and 8Gy

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BioTarget - Ionizing Radiations Effects on Biological Targets

Proton cell irradiation setting

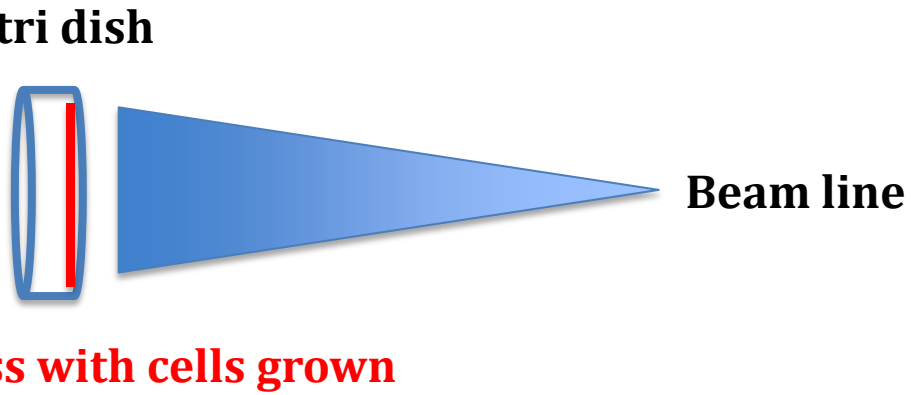
PROTON THERAPY CENTER - Trento

Hs 578Bst cell line irradiated with **protons**. Doses: 2Gy and 8Gy

Proton beam energy: 150MeV

Dose rate: 1.2Gy/min

Beam size: 6cm x 6cm



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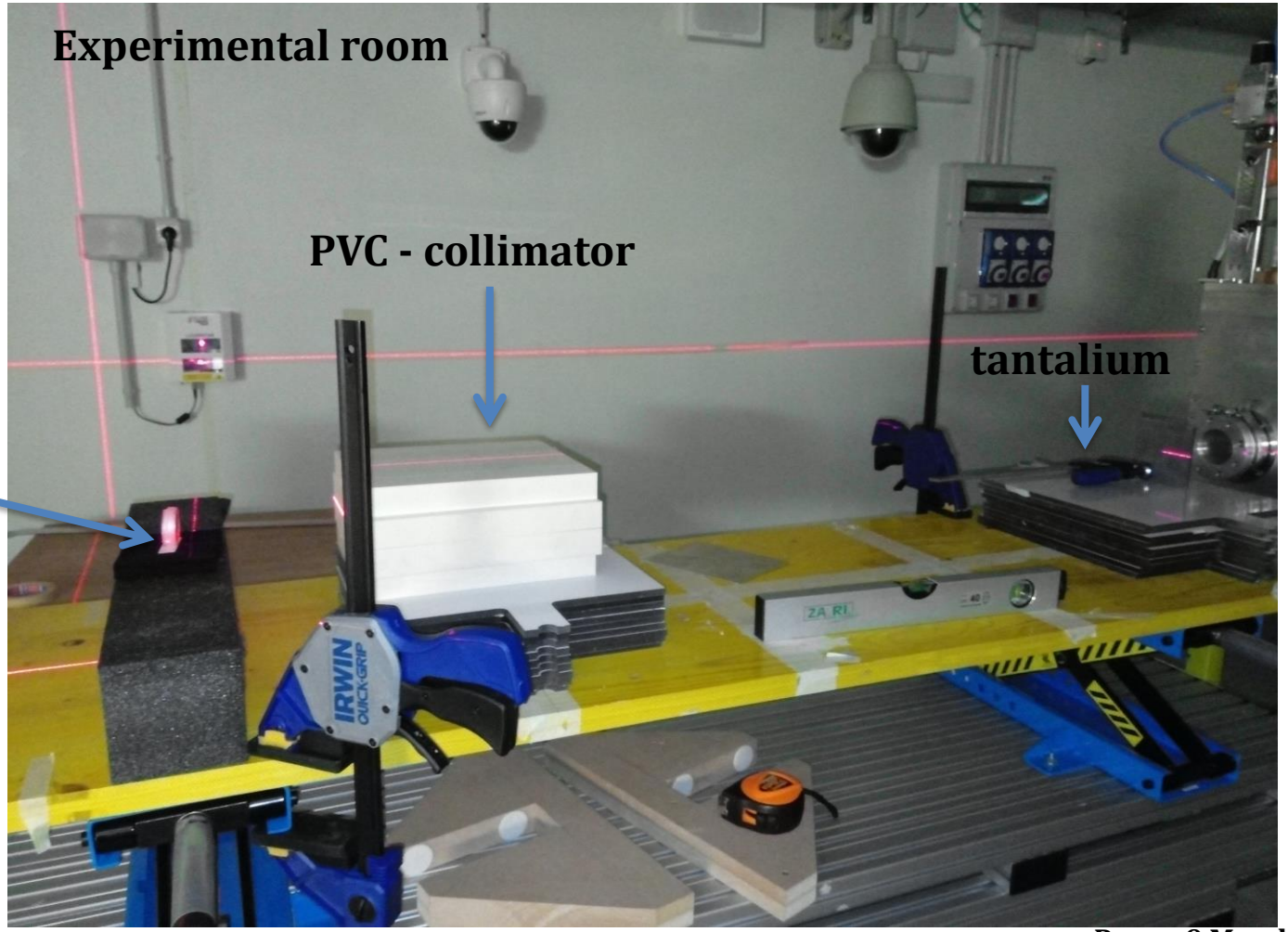

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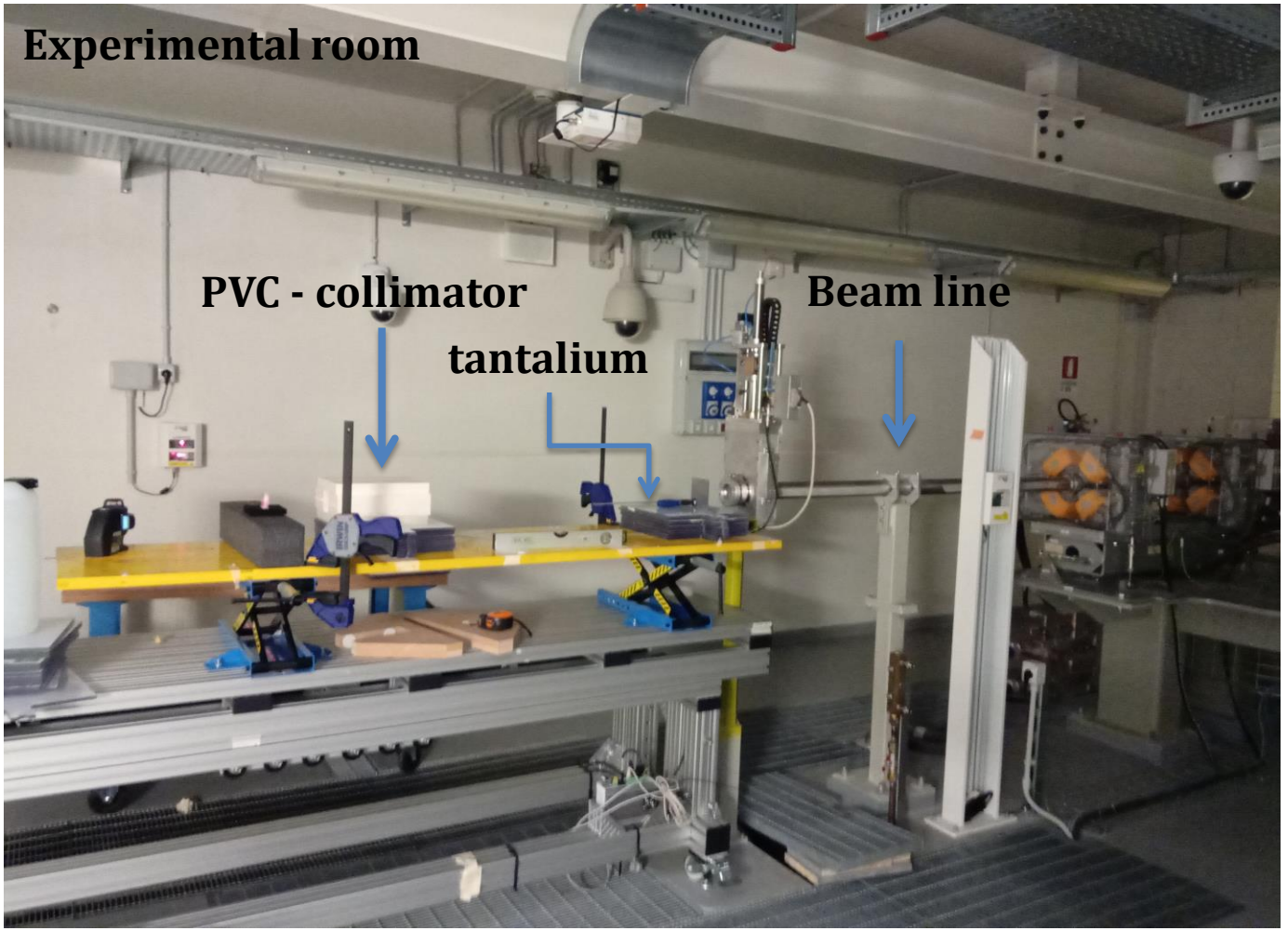

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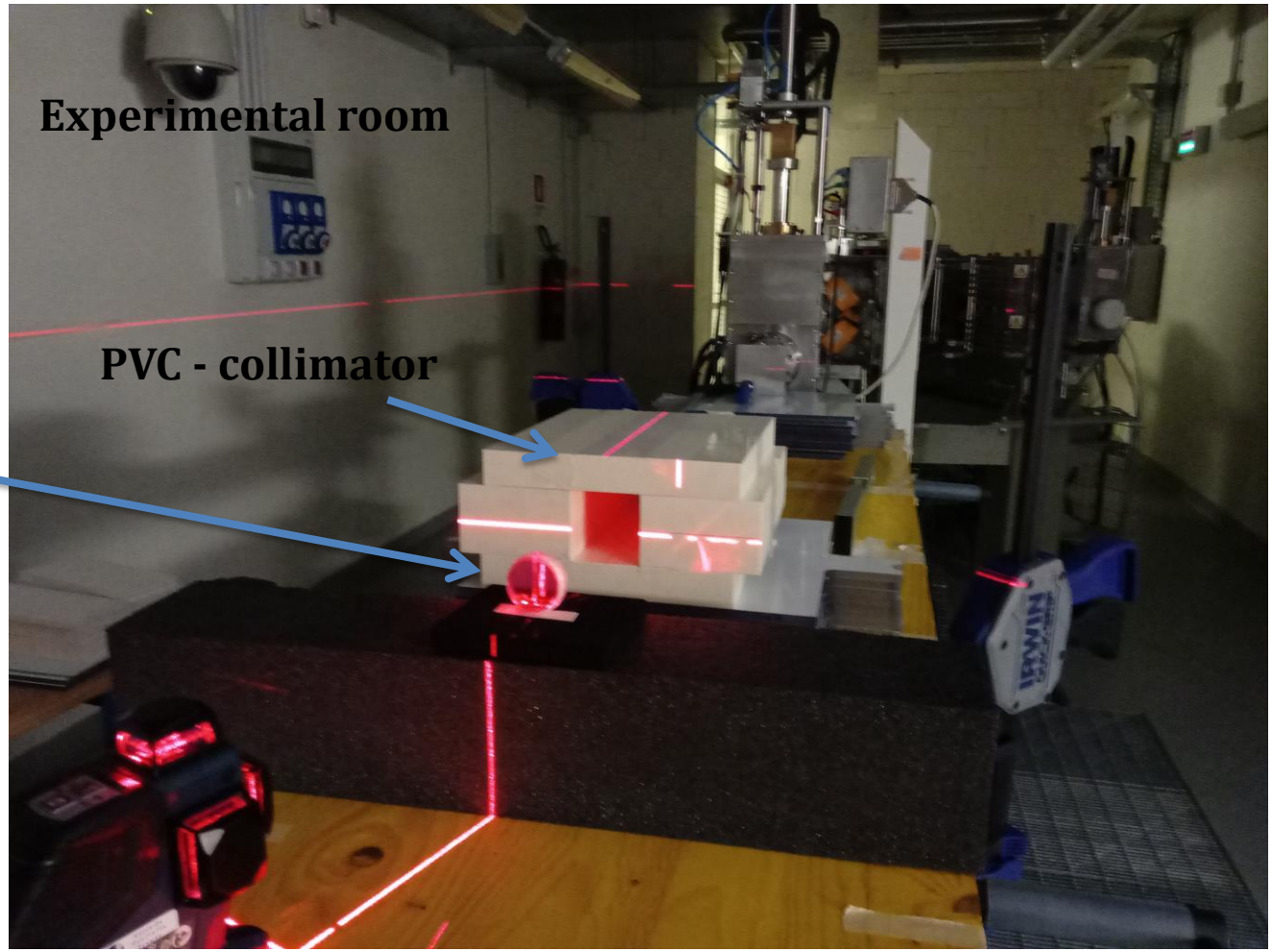

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X – ray cell irradiation setting

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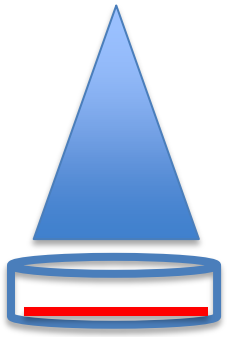
Hs 578Bst cell line irradiated with **X-ray.**
Doses: 2Gy, 8Gy and 25Gy
Intensity 250KVp

X-ray beam



Petri dish **Coverglass with cells grown**

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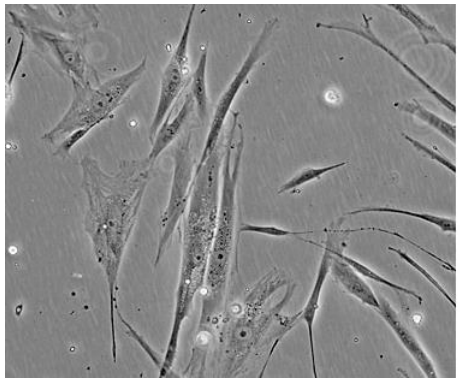
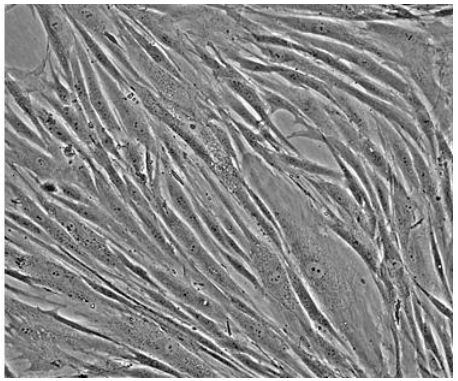
BioTarget - Ionizing Radiations Effects on Biological Targets

Protocol validation of Hs 578Bst cell membrane denaturation





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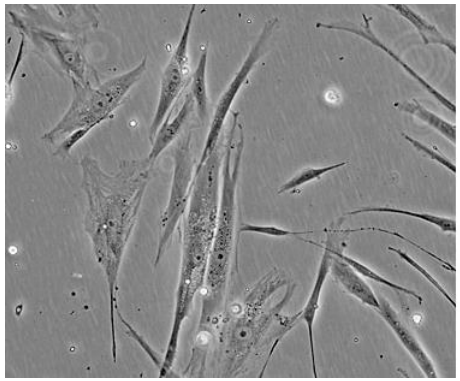
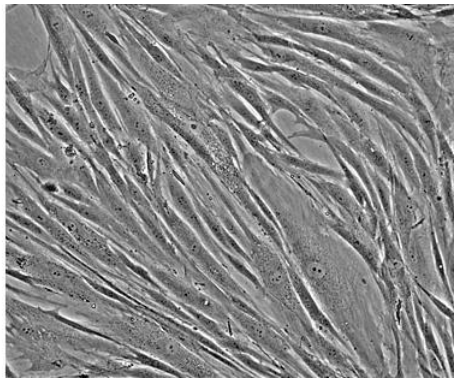
BioTarget - Ionizing Radiations Effects on Biological Targets

Protocol validation of Hs 578Bst cell membrane denaturation

Hs 578Bst cells grow on conventional microscopy cover glasses (21mm x 21mm); 24h later irradiation





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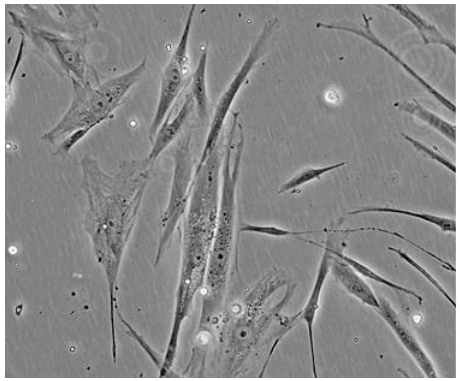
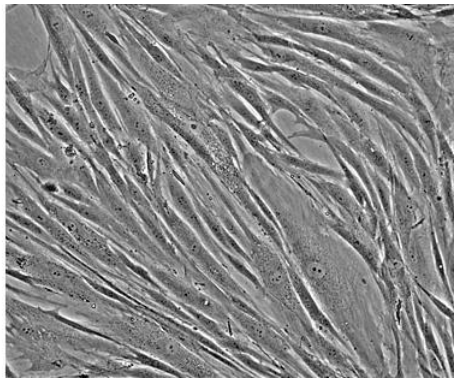
Cell membrane denaturation
(T. Berdyyeva 2005 **102**, 189; 2005) Ultramicroscopy.





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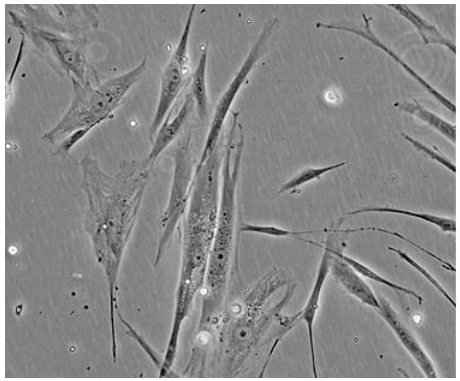

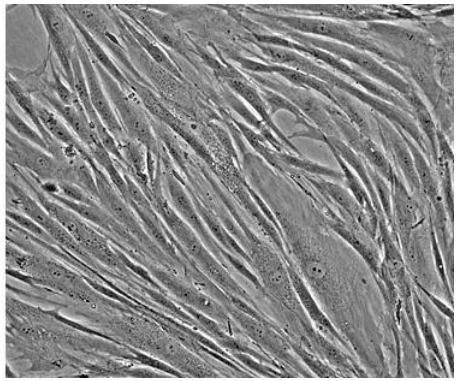

Cell membrane denaturation
(T. Berdyyeva 2005 **102**, 189; 2005) Ultramicroscopy.

Cell fixation (biological cape air flow – 30')

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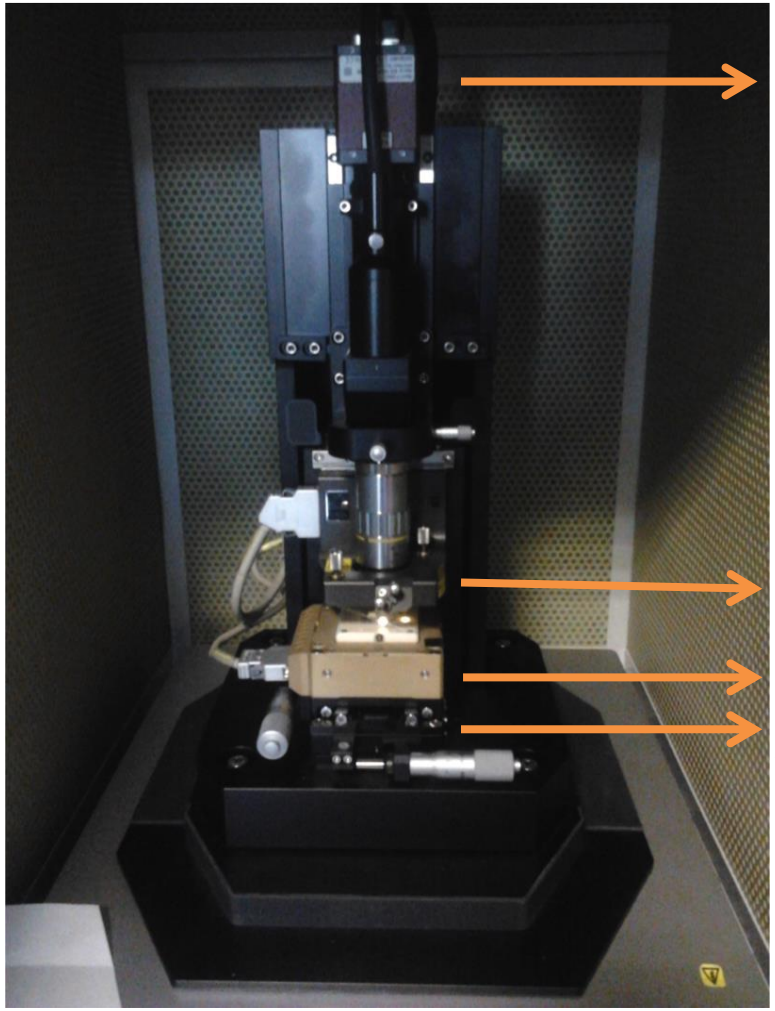
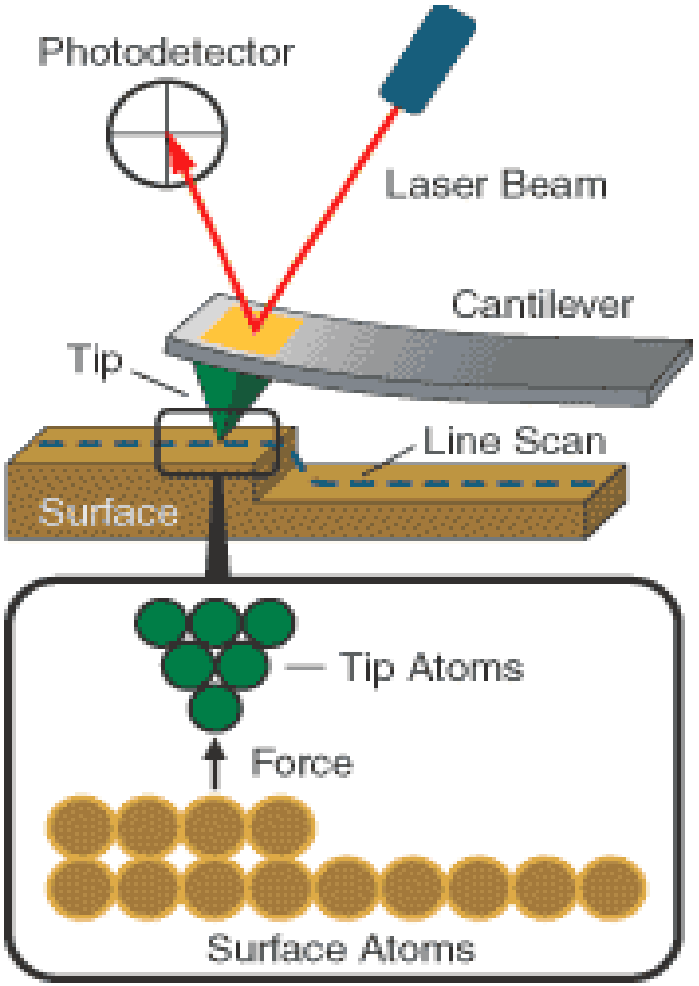
Atomic Force Microscopy measurements





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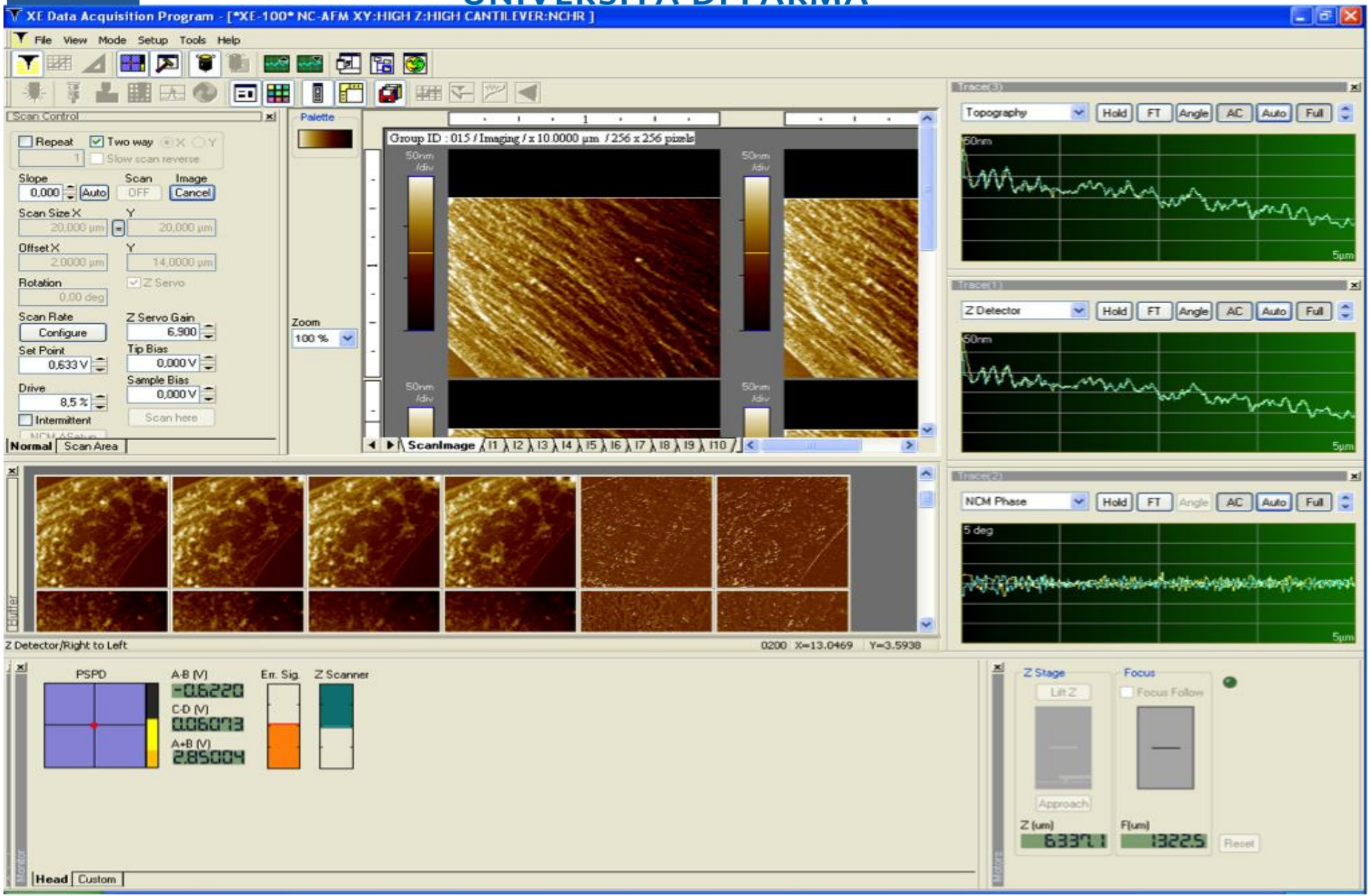

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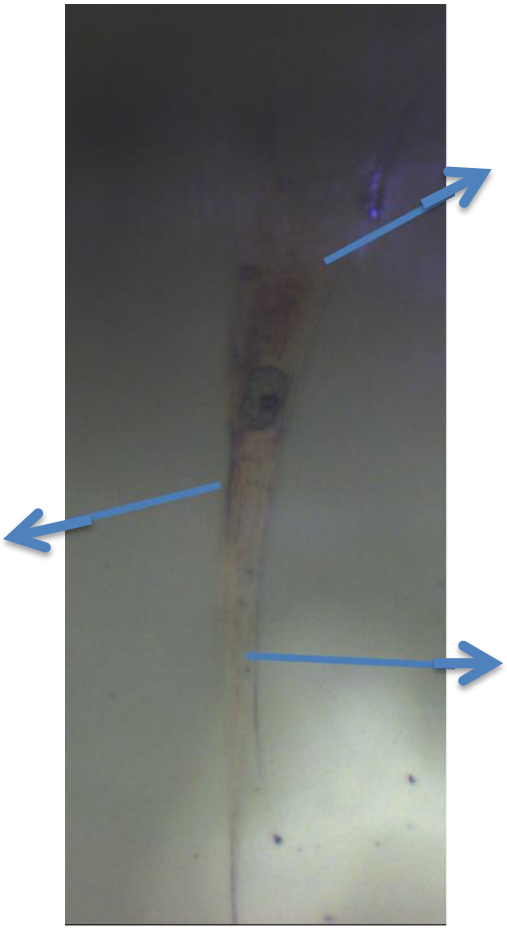
BioTarget - Ionizing Radiations Effects on Biological Targets

Control Hs 578Bst

Atomic Force Microscopy measurements (non contact – air)



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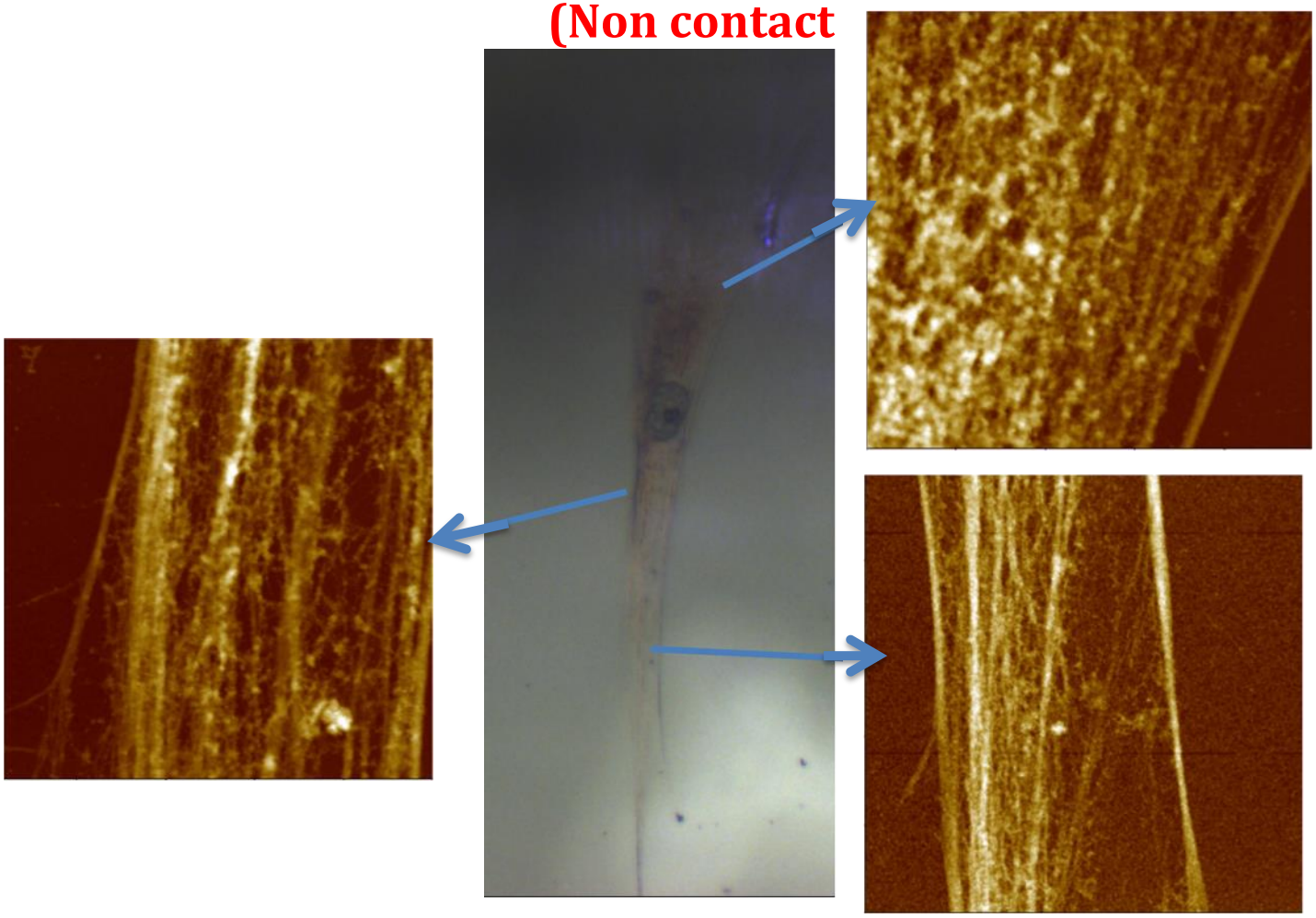

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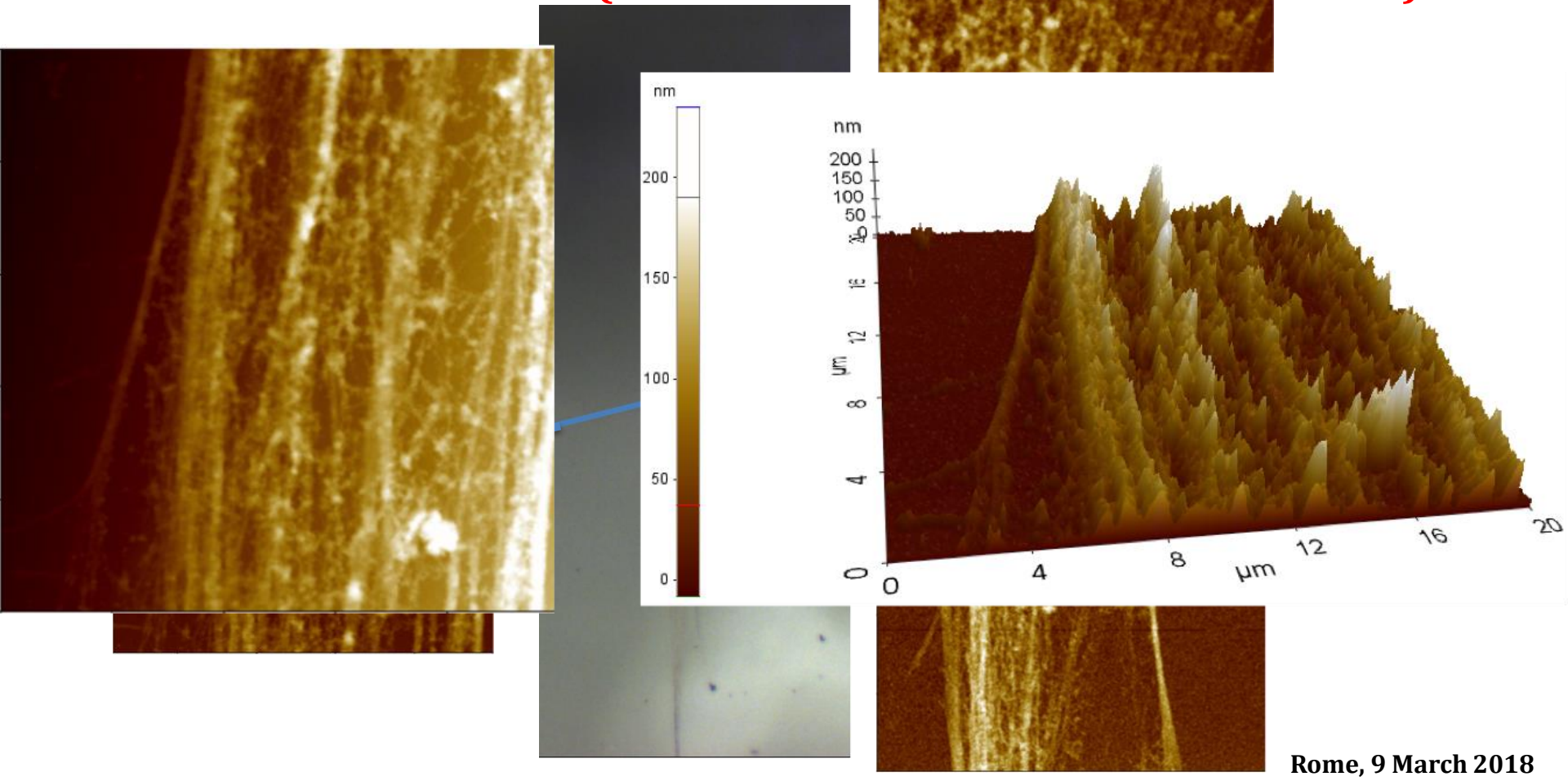

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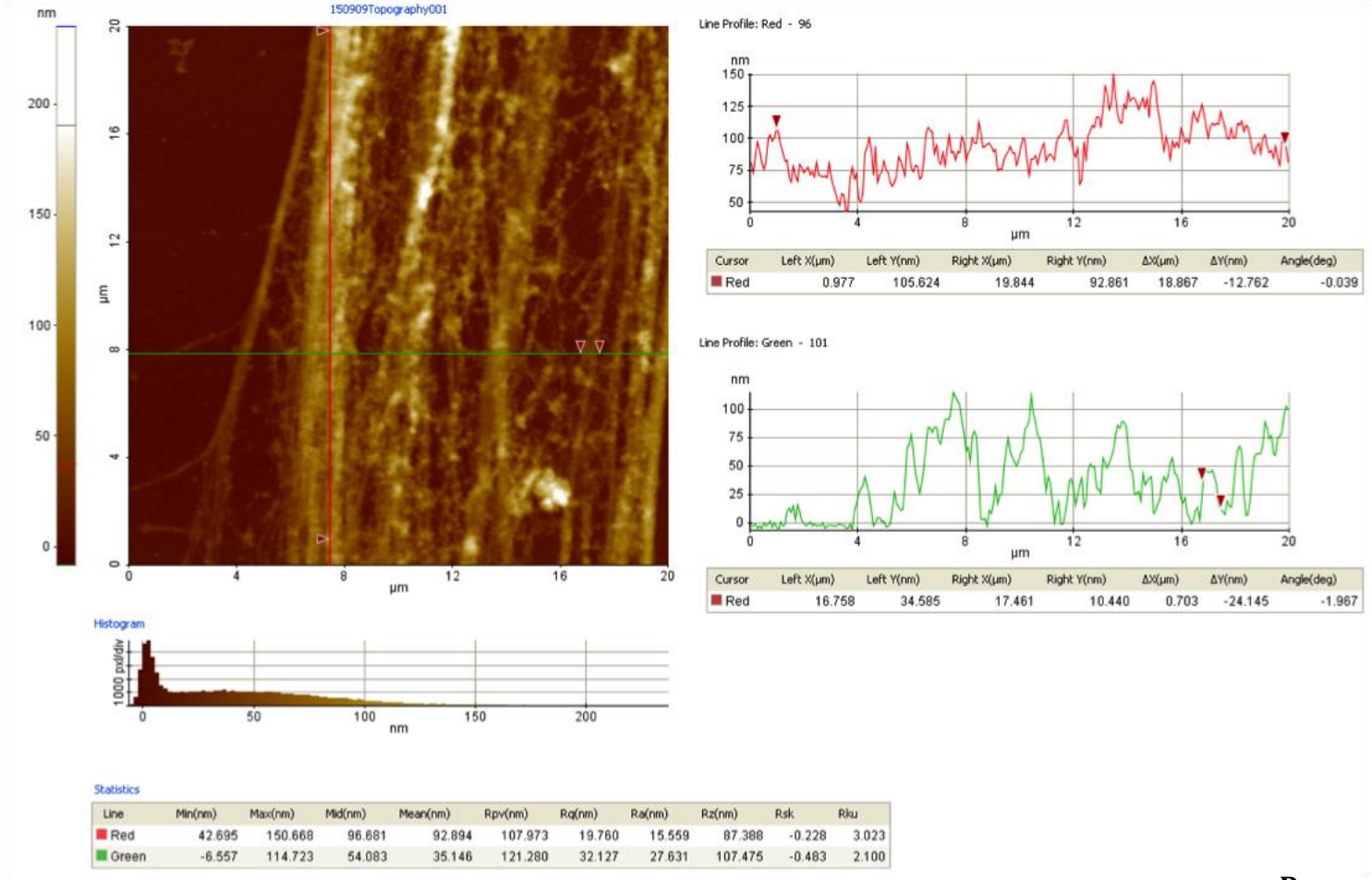

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Control Hs 578Bst Atomic Force Microscopy measurements

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Control Hs 578Bst

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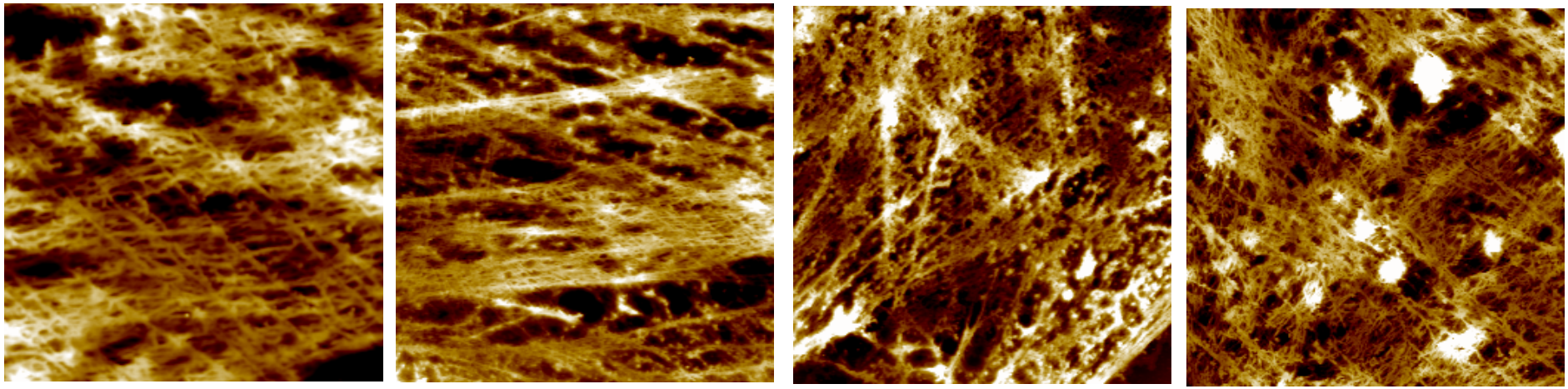

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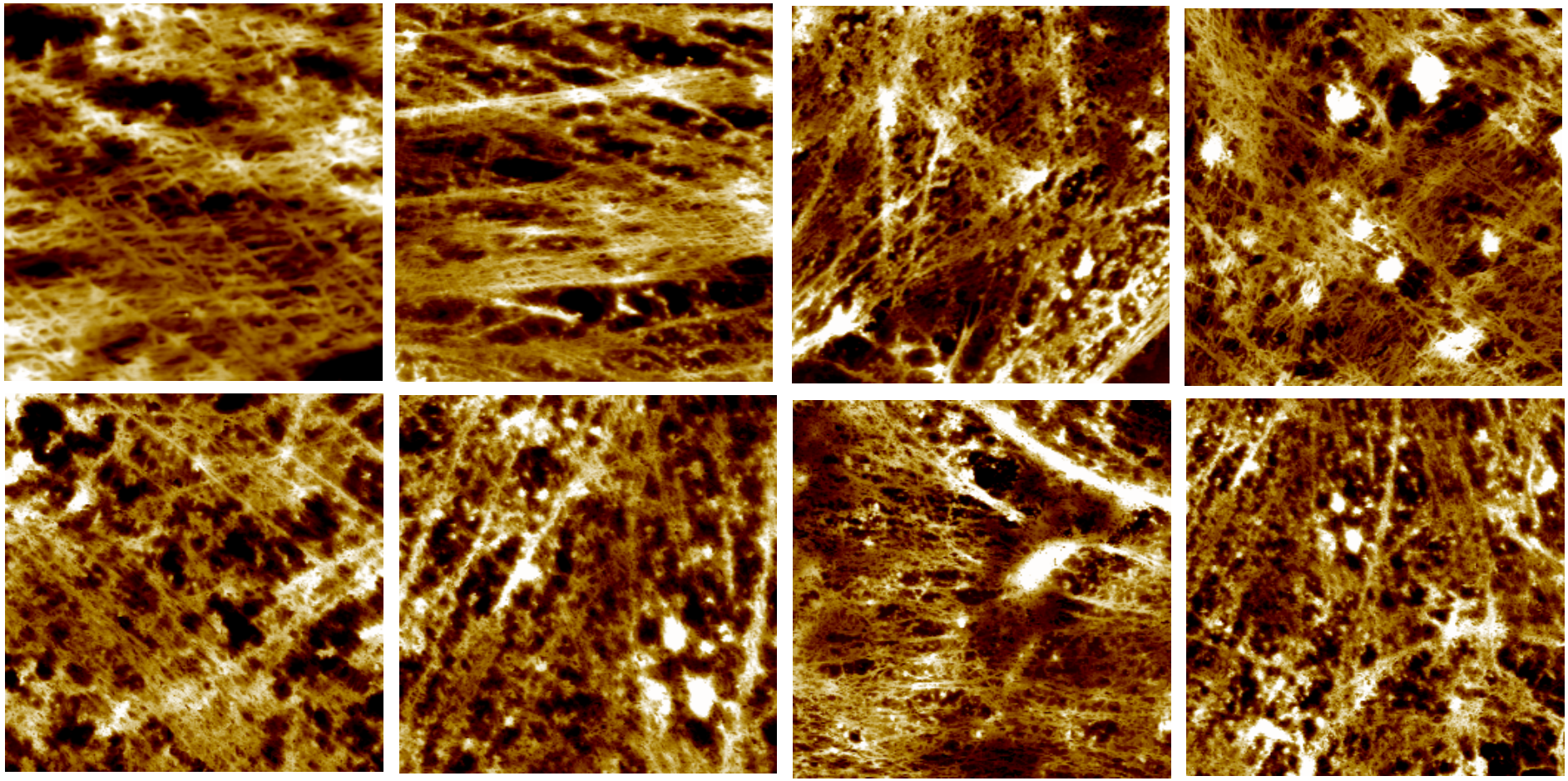

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8Gy protons Hs 578Bst Atomic Force Microscopy measurements

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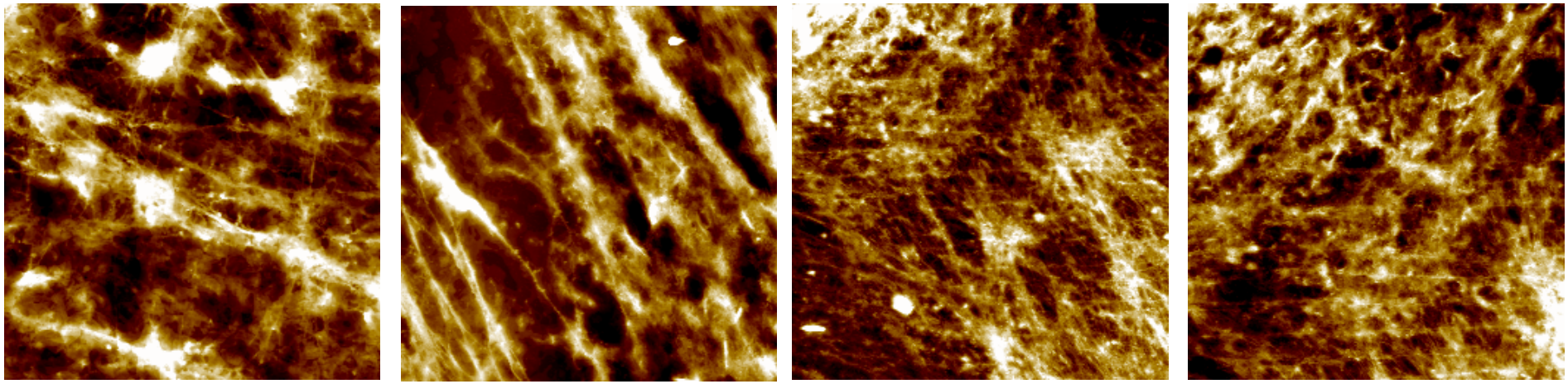
8Gy protons Hs 578Bst Atomic Force Microscopy measurements



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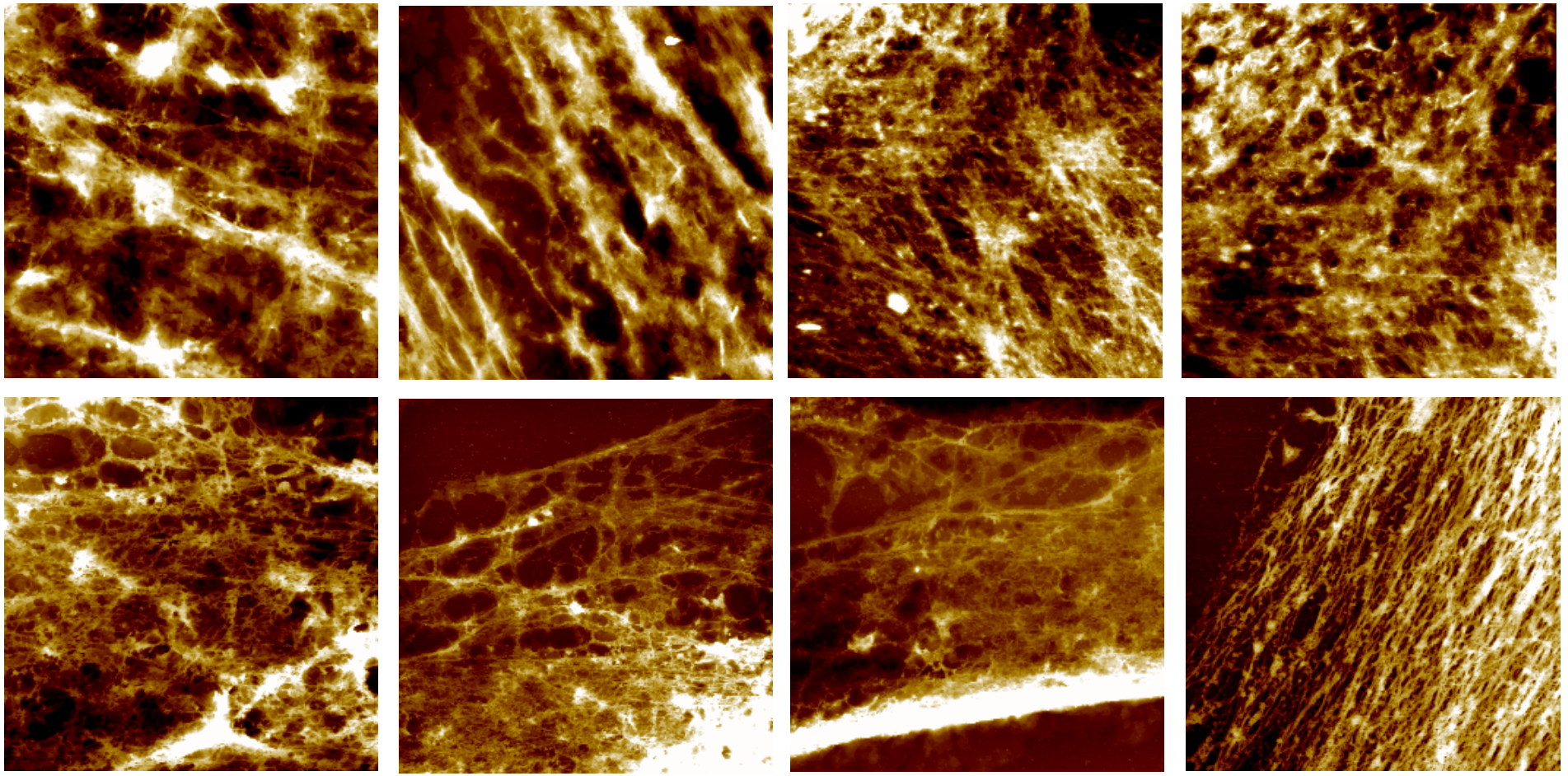

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BioTarget - Ionizing Radiations Effects on Biological Targets

Computational analysis of the samples

Hough Transform

- **Method to identify regions with defined geometrical shape**:
  - layout determination of geometrical shapes;
  - it is possible to recognize straight segments;
  - assessment of fibres density and connectivity

- **Procedure:**
  - isolation of relevant structures;
  - morphological transformation to delete spurious structures;
  - evaluation both number and length of straight segments.

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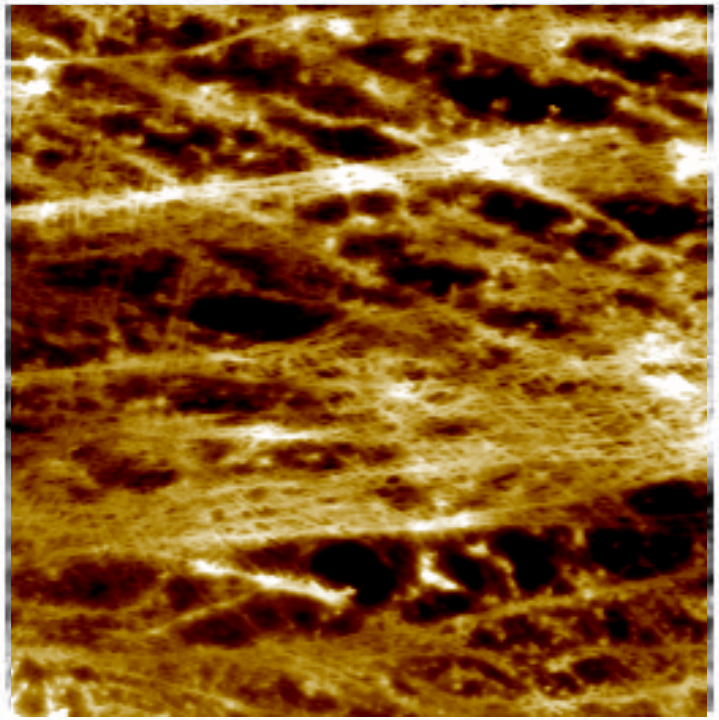
Computational analysis of the samples through parameter

Hough Transform



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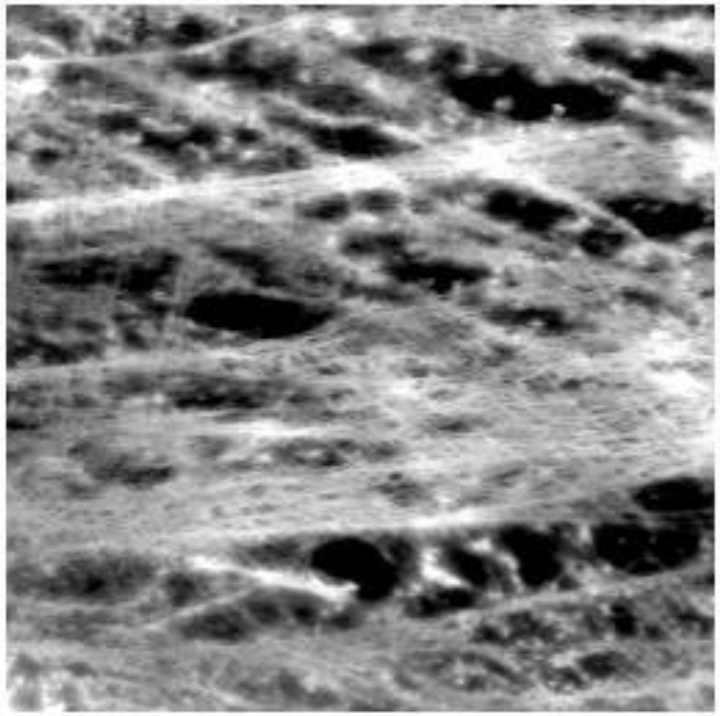

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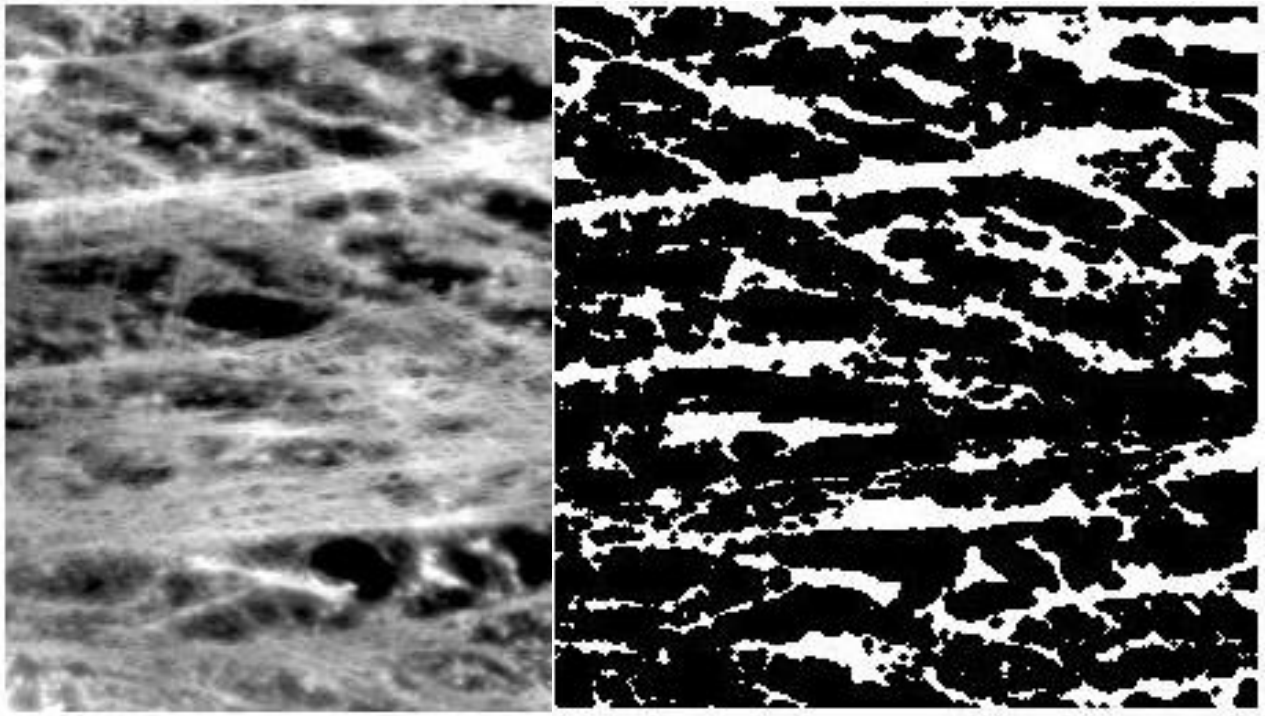

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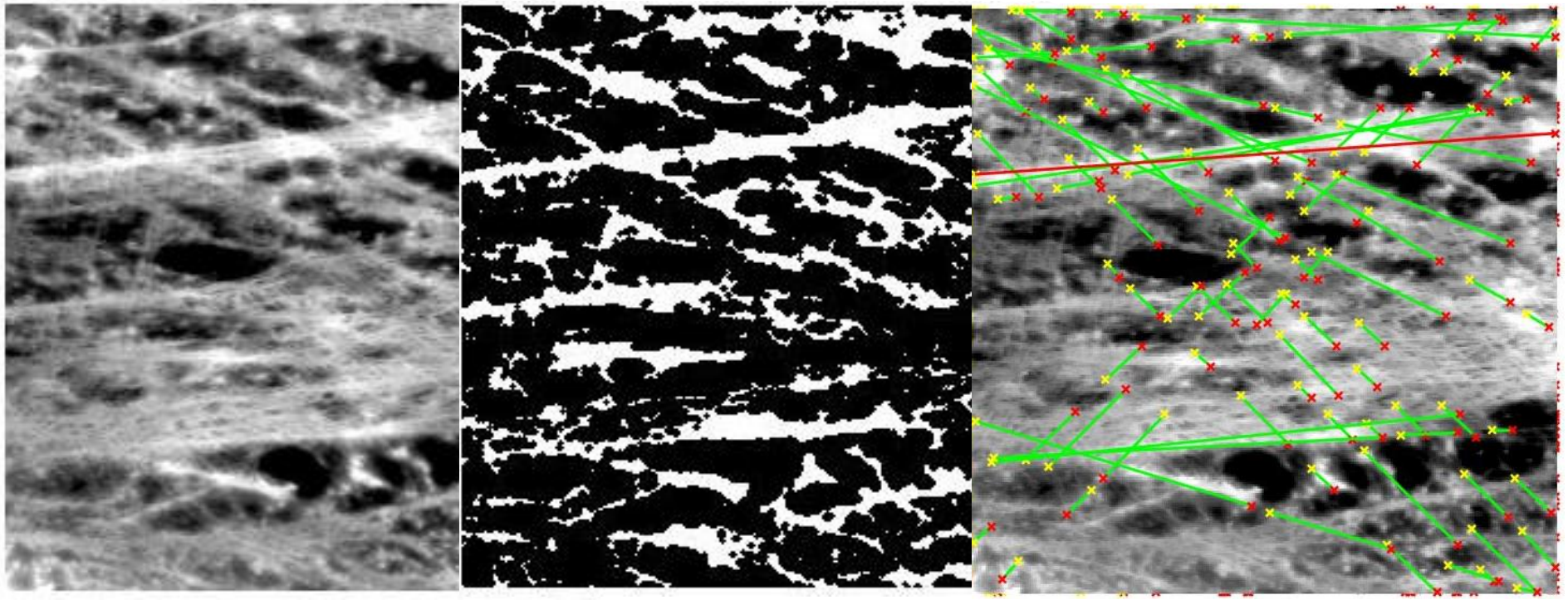

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EXPERIMENTAL GOALS 2018 – 2019: to explore plasmatic membrane and cell cytoskeleton as biological targets of ionizing radiations.

- Quantification of cytoskeleton and membrane damages into irradiated cells to possibly use them as conceivable dosimetric parameters.

- Investigation on cytoskeleton damage of **Hs 578T** cell line (human breast cancer cell line) and possible involving into cancel cell invasiveness.

- Possible use of K^+ biosensor to detect if irradiation leads Hs578Bst cell line to K^+ leakage – G4 as K^+ biosensors and oncogenic regulators.
  (Centro Fermi supports 2014 – 2017)

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2017 meeting and conference:

19th IUPAB congress and 11th EBSA congress "**G-quadruplex: G-rich DNA sequences like potassium biosensor" - poster**

103° Congresso Nazionale della Società Italiana di Fisica, Trento 11 – 15 Settembre 2017
"A view of DNA short sequences rich in guanines like potassium biosensor" – communication.

Pubblication:

Bruni L. et al: PS2.M: Looking for a potassium biosensor. EPJPlus - 2017 Undereview)

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