A radiobiological experiment on breast cancer cell line using laser driven electron accelerators

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THE IBFM TRANSLATIONAL RESEARCH MODEL

Diagnosis
Molecular imaging by MRI, PET/CT

Disease Unit

Therapies
EBRT, IORT, Hadrotherapy

Prognosis/Prediction
Cell-based monitoring response to therapies
Breast cancer (BC) is a very complex, multifactorial disease, highly heterogeneous at a molecular and clinical level and presents distinct subtypes (>30) associated with different clinical outcomes.

- BC affects 1 out of 8 women during their lifetime and represents 29 % of all cancers affecting women.

- To treat BC radiation therapy (RT) plays an important role, often used in combination with surgery and chemotherapy.
There are a large number of immortalized cell-lines available as study models for BC. Neve RM et al.  *Cancer Cell*, 2006
Biological effects induced by IR have been studied by *in-vitro, ex-vivo* and *in-vivo* approaches and by the integration of **multidisciplinary skills** of biologists, physicists, engineers and physicians of our group.

The principal *in-vitro* activities have been carried out on **breast cancer cell lines**, immortalized and primary cells from patient tumour biopsies (*ex-vivo*) with different beams:

- **electrons**,
- **protons** and
- **electrons produced by laser plasma interaction**.
Main goal is to highlight molecular mechanisms, by OMIC approach, involved in the response to radiation treatment with different types of beam, in order to identify radiosensitivity/radioresistance biomarkers and personalize treatments.

**IN VITRO/EX VIVO CELL-BASED MODELS**

- Gene expression profiling by Microarray
- Immunofluorescence
- Morphology and vitality assays
- qRT-PCR
- Luminex
- Western Blot
- Proteomics
Cell and molecular response to IR is highly complex, dependent on: LET, dose rate, dose fractionation, radiation dose and type of the irradiated cells or tissues (Hellweg CE, Spitta LF et al. Front Oncol 2016 ;6:61).


Minafra L and Bravata V. Transl Cancer Res 2014; 3 (1):32-47
Molecular models of response to high dose electron RT

MCF7 breast cancer cell line

MCF10A normal breast cell line

In the cellular response to radiation, the activation of several signal transduction pathways by IR, results in an altered expression of a series of target genes, defining in cell death or survival.

Bravata V, Minafra L et al.
Anticancer Res 2015;35(5):2577-91

Minafra L, Bravata V et al.
Anticancer Res. 2015; 35(6):3223-34
RADIOBIOLOGICAL LASER DRIVEN EXPERIMENT
RADIOBIOLOGICAL LASER DRIVEN EXPERIMENT

MCF7 BC cell line
By infiltrating ductal carcinoma

Electron beam | LDA (ILIL)
---|---
D/pulse | 0.07 Gy/pulse
Dose rate | 4 Gy/min
$t_{\text{pulse}}$ | $10^{-12}$ s
Peak dose rate | $7 \times 10^{10}$ Gy/s
Energy | up to 20 MeV
Frequency | 0.5 Hz
EBRT ON MCF7 BC CELL LINE

<table>
<thead>
<tr>
<th>D (Gy) (± SD)</th>
<th>EBRT SF (± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.40 ± 0.01</td>
<td>0.85 ± 0.03</td>
</tr>
<tr>
<td>2.0 ± 0.1</td>
<td>0.65 ± 0.02</td>
</tr>
<tr>
<td>3.7 ± 0.1</td>
<td>0.24 ± 0.03</td>
</tr>
<tr>
<td>5.9 ± 0.2</td>
<td>0.15 ± 0.02</td>
</tr>
<tr>
<td>8.4 ± 0.3</td>
<td>0.014 ± 0.001</td>
</tr>
</tbody>
</table>

Dose rate: 2 Gy/min
T\text{pulse}: 10^{-6} \text{ s}
Energy: 6 \text{ MeV}
LDA VS EBRT ON MCF7 BC CELLS

<table>
<thead>
<tr>
<th>D (Gy) (± SD)</th>
<th>EBRT SF (± SD)</th>
<th>LDA SF (± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8 ± 0.1</td>
<td>0.63 ± 0.02</td>
<td>0.19 ± 0.01</td>
</tr>
<tr>
<td>3.2 ± 0.2</td>
<td>0.38 ± 0.04</td>
<td>0.17 ± 0.02</td>
</tr>
<tr>
<td>4.4 ± 0.3</td>
<td>0.22 ± 0.03</td>
<td>0.07 ± 0.01</td>
</tr>
<tr>
<td>5.4 ± 0.3</td>
<td>0.14 ± 0.02</td>
<td>0.06 ± 0.01</td>
</tr>
<tr>
<td>6.9 ± 0.4</td>
<td>0.06 ± 0.01</td>
<td>0.04 ± 0.01</td>
</tr>
<tr>
<td>7.4 ± 0.5</td>
<td>0.05 ± 0.01</td>
<td>0.03 ± 0.01</td>
</tr>
</tbody>
</table>
CONCLUSION

- Our radiobiological experiment with laser electron beam represents the first one performed on MCF7 BC cell line.

- Further studies and experiments are needed to improve laser technology and to better understand the biological effects regarding both ultra-short duration of particle bunches and the extremely high dose rate released.
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