CT Scan longitudinal study for hepatocellular carcinoma treatments efficiency

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Hepatocellular carcinoma:
- 3rd most deadly cancer in the world
- limited effects of current therapy

Previous studies show efficiency of two types of treatment:
- proteins inhibitors
- epigenetic agents

**Objective:** combine these oncogenes with immunotherapy (targeting immune checkpoints) to boost immune system
DePlcT project

The DePlcT concept

Contrast agents (barium, iodine, gold)

PIXSCAN-FLI
Spectral CT-Scan

Energy thresholds
Hybrid pixels

- Multiplexing
- High cadence

Immunotherapy + Anticancer drugs

Anticancer treatment evaluation
Tumor progression / regression
Microenvironment remodeling

3D volumes
3D concentrations of separated components

Longitudinal imaging of liver cancers

http://imxgam.in2p3.fr/depict.php

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X rays:
- from 40 to 150 kV
- filter wheel
PIXSCAN-FLI

Animal support:
- 3-axis motion + rotation
- gas anesthesia system

X rays:
- from 40 to 150 kV
- filter wheel
Detector:
- Si 500 µm
- hybrid pixels 130x130 µm²

Animal support:
- 3-axis motion + rotation
- gas anesthesia system

X rays:
- from 40 to 150 kV
- filter wheel
In vivo imaging protocol

- Standard absorption imaging
- Source: 50 kV/500 µA/0.6 mm Al
- Data acquisition mode: continuous
- Pose duration: 575 ms + 50 ms DT
- Projections: 720 (0.5°)
- Delivered dose: 180 mGy/acquisition

Hepato-specific contrast agent based on barium nanoparticles
  - -> enhance liver contrast
  - -> Ideal for longitudinal studies

Coronal slices of a mouse images before, one day after and three weeks after injection of Exitron nano 12000
Protocol

1\textsuperscript{st} cohort

2\textsuperscript{nd} cohort
Protocol

1\textsuperscript{st} cohort

Decitabine + anti PD-L1 + anti CTLA-4

2\textsuperscript{nd} cohort

BCL-XL + MEK + anti PD-L1 + anti CTLA-4
Protocol

1st cohort

D0*

D10*

D20*

Decitabine + anti PD-L1 + anti CTLA-4

BCL-XL + MEK + anti PD-L1 + anti CTLA-4

2nd cohort

* Longitudinal study with PIXSCAN-FLI prototype

Contrast agent

Tumoral volume quantification

➤ Tumor evolution (1)

➤ Volume measurement (1)
Protocol

1\textsuperscript{st} cohort

2\textsuperscript{nd} cohort

Decitabine + anti PD-L1 + anti CTLA-4

BCL-XL + MEK + anti PD-L1 + anti CTLA-4

* Longitudinal study with PIXSCAN-FLI prototype

Tumoral volume quantification

- Tumor evolution (1)
- Microenvironment remodeling (2)

Contrast agent

Volume measurement (1)
Protocol

1\textsuperscript{st} cohort

\[ \text{D0*} \quad \text{D10*} \quad \text{D20*} \]

Decitabine + anti PD-L1 + anti CTLA-4

Flow cytometry (3)
- Immune cells population analysis

2\textsuperscript{nd} cohort

\[ \text{D0*} \quad \text{D10*} \quad \text{D20*} \]

BCL-XL + MEK + anti PD-L1 + anti CTLA-4

\* Longitudinal study with PIXSCAN-FLI prototype

Contrast agent

- Tumor evolution (1)
- Microenvironment remodeling (2)

Tumoral volume quantification
- Volume measurement (1)

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Results – Imaging (1)

Heterogeneous treatment response
- More important regression for the 2nd cohort
Results – Imaging (1)

Heterogeneous treatment response
➢ More important regression for the 2\textsuperscript{nd} cohort

Tumoral regression after 20 days of treatment

Tumoral regression during treatment – 1\textsuperscript{st} cohort

Tumoral regression during treatment – 2\textsuperscript{nd} cohort
Results – Imaging (1)

Heterogeneous treatment response
➤ More important regression for the 2\textsuperscript{nd} cohort
Results – Imaging (2)

Tumoral microenvironment remodeling

- Immune cells accumulation on the tumor area

Initial heterogeneity, different tumoral « classes »

Tumor evolution examples (at D0 in the left and D20 in the right)
Results – Flow cytometry (3)

Immune cells recruitment:
- Differences of number of recruited cells
- Cells population of innate immunity different for both treatments
Results – Flow cytometry (3)

Immune cells recruitment:
- Treatment of the 1\textsuperscript{st} cohort allows a better recruitment of adaptative immunity
Conclusion and perspectives

- Longitudinal study carried out from the tumor analysis to the immune cells analysis
- **Important differences** between both treatments: different action mechanisms
- Huge **heterogeneity** of tumors and response

- Understand correlations between tumoral regression and immune cells populations
- Study recruitment of immune cells at different steps

- A better understanding of tumors heterogeneity will allow to **adapt specifically the treatment**
Thank you for your attention

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