Development of a prediction model of local response for oligometastatic patients treated by cranial and extracranial stereotactic radiotherapy

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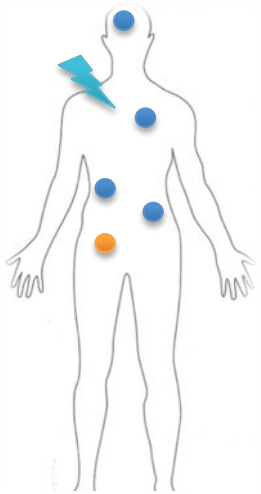
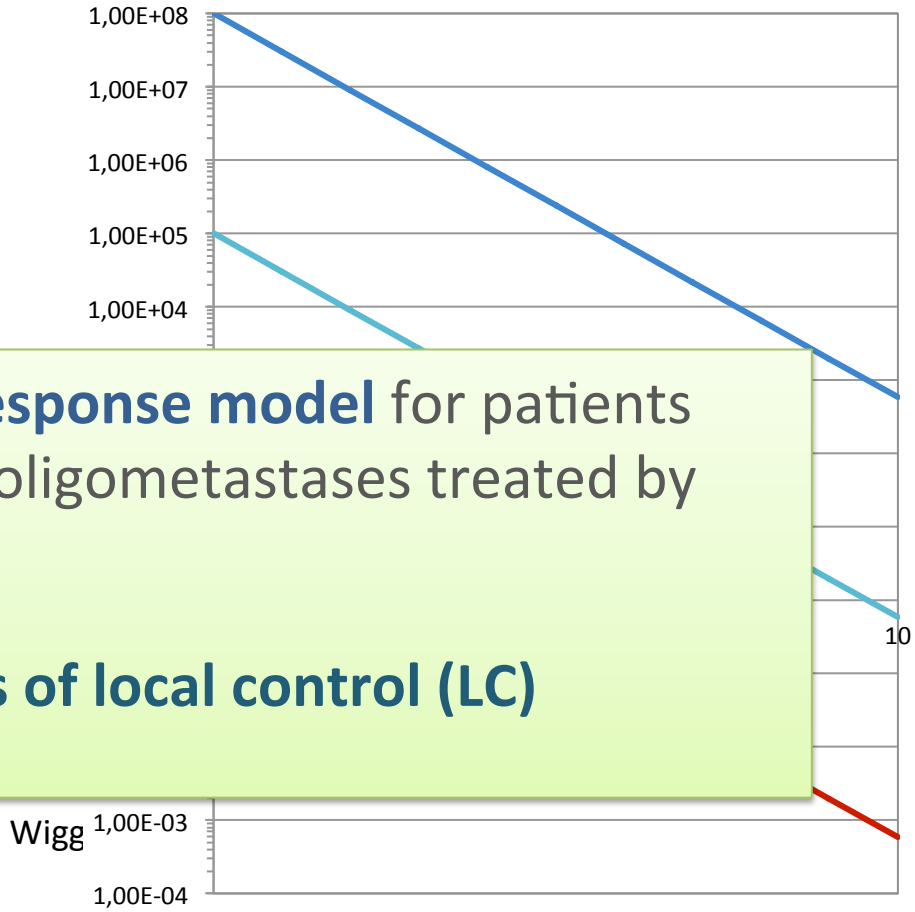
Background



- **local control** of oligometastases may result in improved systemic control and prolonged survival
- **SBRT/SRS:** target dose escalation (tumor control), minimizing normal tissue exposure

The Dose

SRS for **intracranial** metastases leads to longer pts survival, local control and mantained functional status (vs WBRT alone); local control is highly dependent upon dose (> 80% after 21 Gy or >)



1. To develop **a dose-volume-response model** for patients with cranial and extracranial oligometastases treated by stereotactic RT
2. To identify **predictive factors of local control (LC)**

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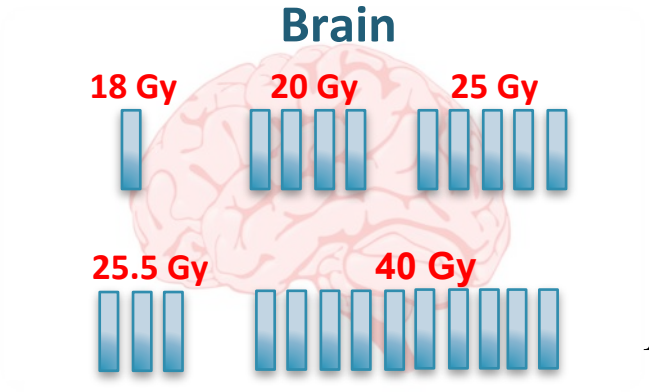
Methods and Materials

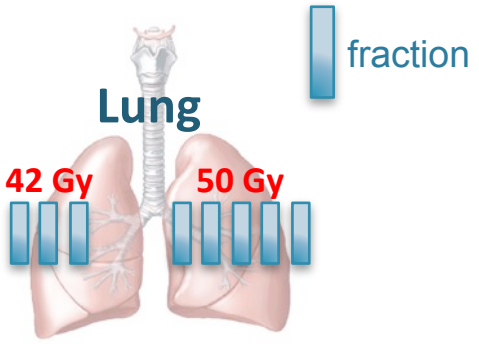
- Clinical data of oligometastatic patients (≤5 metastatic lesions) who received SBRT/SRS at our Institution
- Primary tumors were required to be treated curatively and considered inactive and/or controlled
- FUP ≥ 2 years (CT, MRI and PET-CT scans)
- **Tumor response** evaluated at the time of maximum response according to RECIST criteria (RC, PR, SD, PD)

Red: total dose



$$BED = nd\left(1 + \frac{d}{\alpha/\beta}\right)$$

n: number of fractions
d: fraction dose
α/β=10



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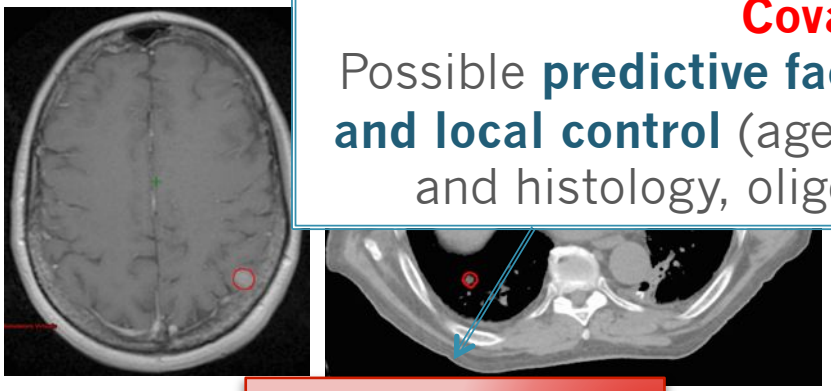
Methods and Materials

Covariates

Possible **predictive factors of tumor response and local control** (age, gender, primary cancer and histology, oligometastatic site, ND)



Tumor Response

$$Vol = \frac{4}{3}\pi\left(\frac{D_1}{2}\right)^3$$

Local Control

$$BED_{10}$$

$$\left[\frac{1}{3}\pi\left(\frac{1}{2}\right)\right]$$

Multivariate Analysis
dose-volume-response model
(logistic generalized linear model)

- **Modeling procedure:** performed using three generalized linear models (Logit, LogLogit and Poisson)
- **Evaluation:** assessed by AIC, Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC) and calibration of the model. The **validation** has been performed using an internal validation technique

Univariate Analysis
Kaplan-Meier

Multivariate Analysis
Cox proportional hazard regression model

lized Dose

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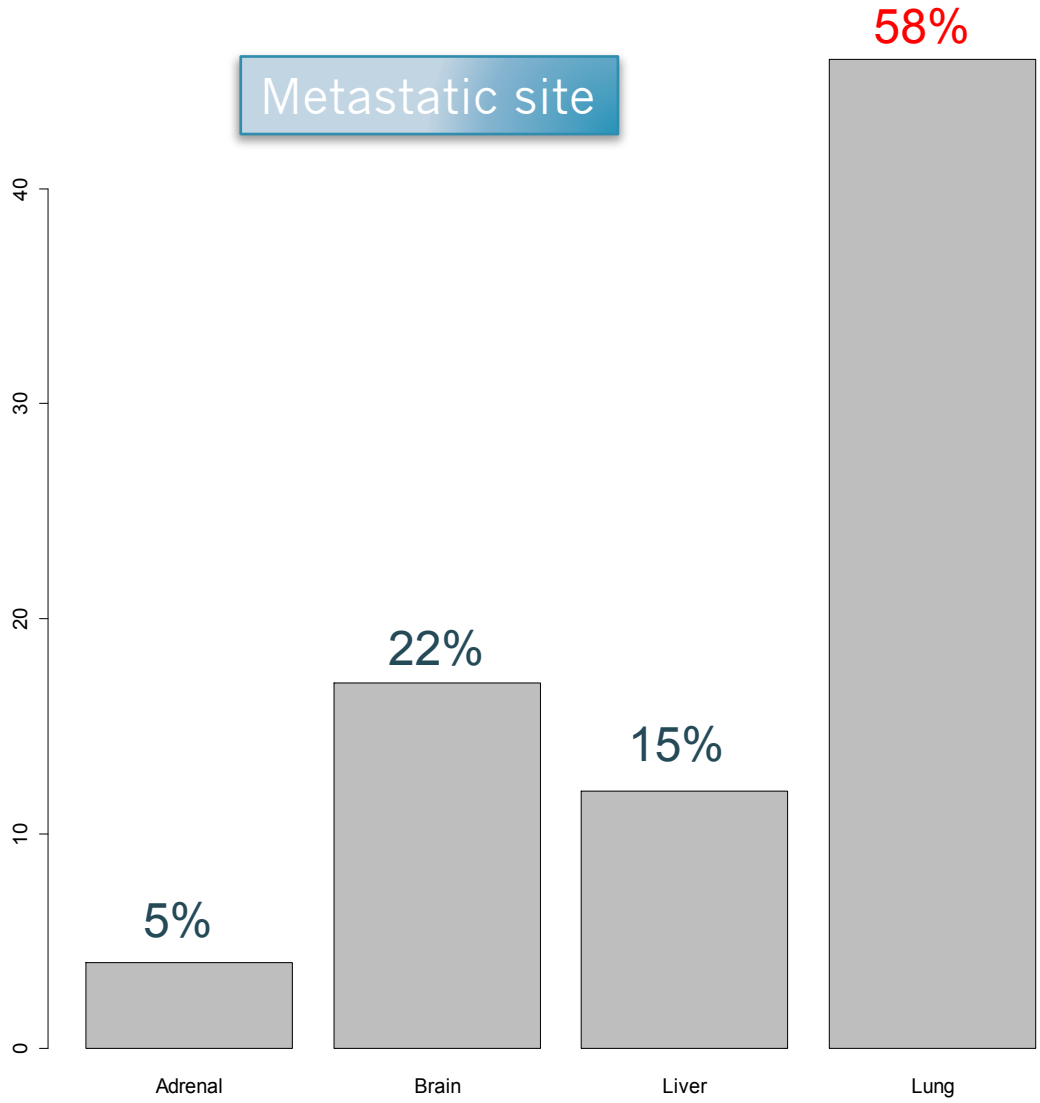
Results

- Between October 2005 and July 2013
- 53/187 assessable patients
- median FUP 33.4 months (30.7~48.8)
- Median age 64 years (32-82)
- **79 metastatic lesions**



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The Dose-Volume-Response Model

CR	33 (42%)
PR	15 (19%)
SD	13 (16%)

Model	TND50	p-value	γ50	p-value	AIC
Logit	16.26	1.996E-15	0.62	0.0006606	97.57
LogLogit	16.09	1.81E-08	0.43	0.005339	97.47
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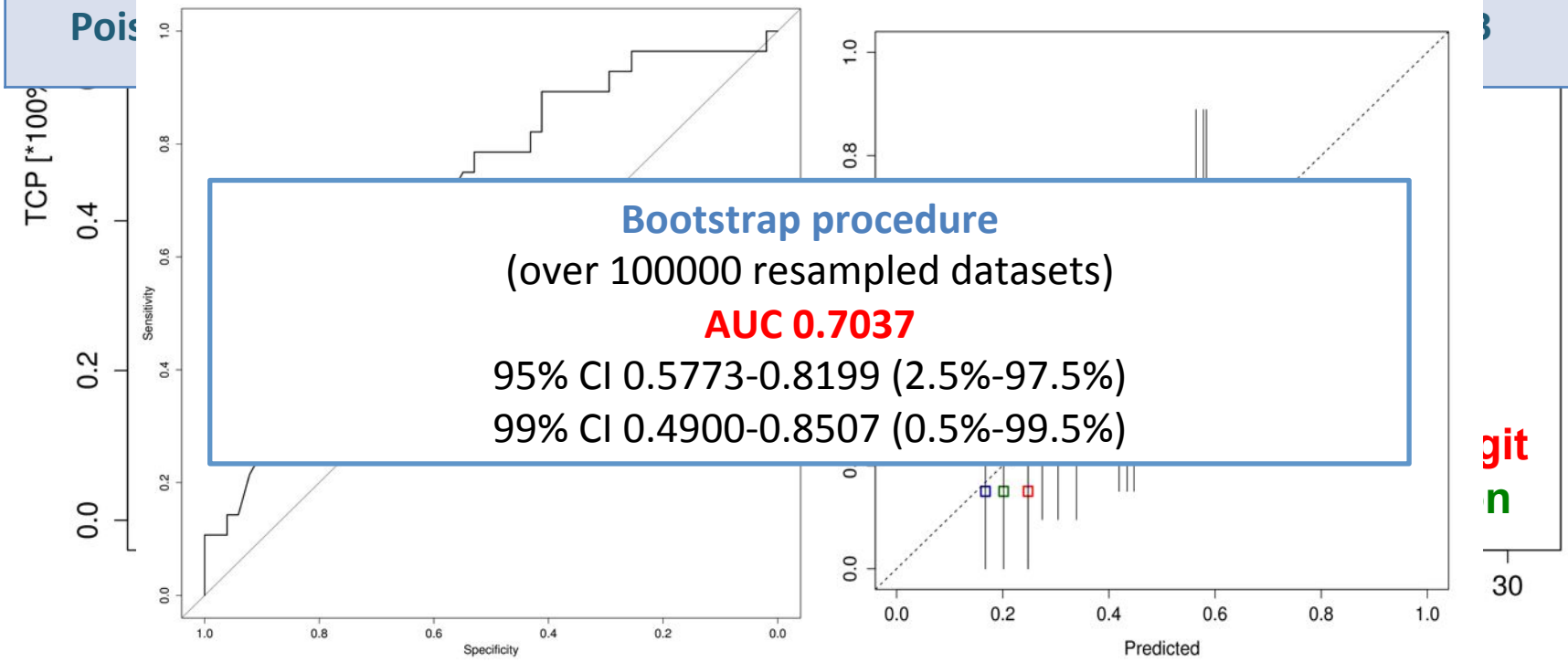

Bootstrap procedure
(over 100000 resampled datasets)
AUC 0.7037
95% CI 0.5773-0.8199 (2.5%-97.5%)
99% CI 0.4900-0.8507 (0.5%-99.5%)

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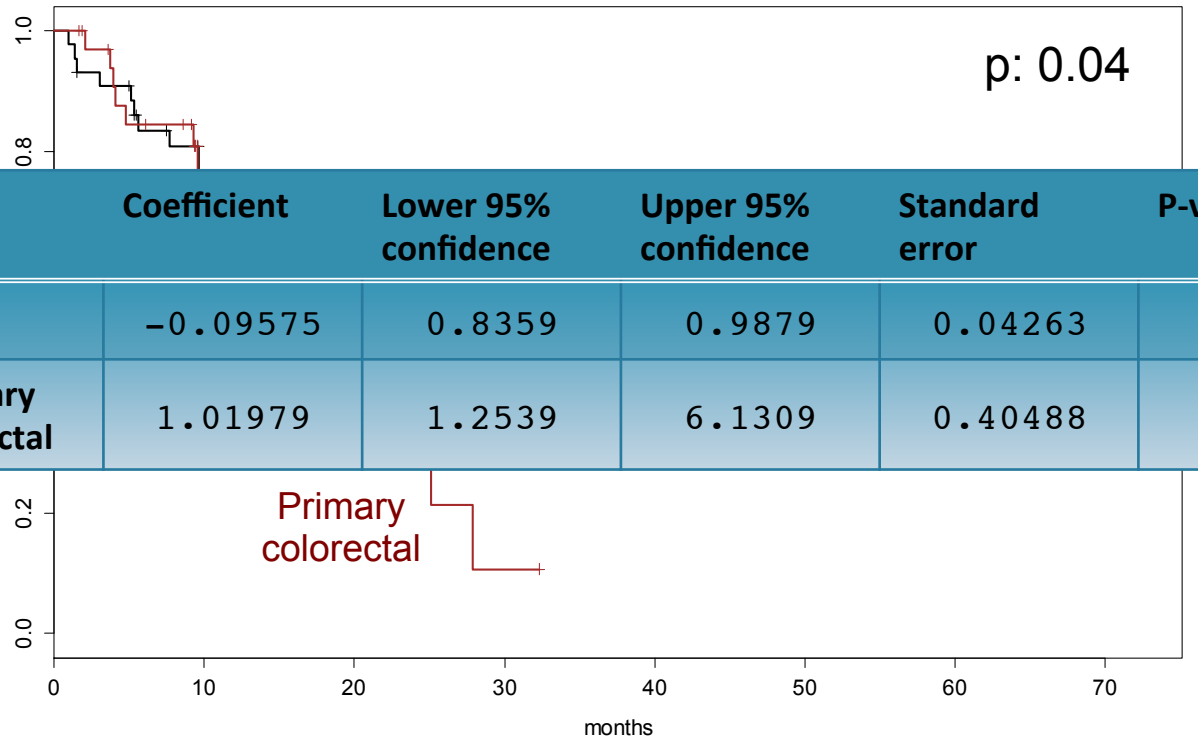
Results

Median LC 27.9 months (23.7~NA)
LC-2yr 60%



Factor	Coefficient	Lower 95% confidence	Upper 95% confidence	Standard error	P-value
ND	-0.09575	0.8359	0.9879	0.04263	0.0247
Primary Colorectal	1.01979	1.2539	6.1309	0.40488	0.0118

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Conclusions

- The **dose-volume-response model** shows a significant relationship between the prescribed **dose**, the lesion **volume** and the **tumor response**
- The **performance** was good and the **internal validation** was successful
- It requires an **external validation** to assist fisicians in treatment decision making
- Ongoing **prospective evaluation**

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