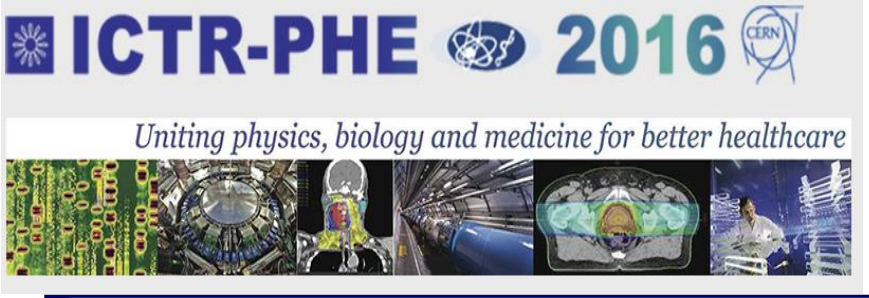


France HADRON

The use of radiobiological TCP and NTCP models to validate the dose calculation algorithm and readjust the prescribed dose

Abdulhamid Chaikh[1], Jean-Pierre Bresciani[2], Jacques Balosso[1,3]

[1]Department of Radiation Oncology and Medical physics, University Hospital of Grenoble, France.
[2]University of Fribourg Department of Medicine, Switzerland.
[3]Grenoble-Alpes University, France.

E-mail: abdulhamedc@yahoo.com & Jbalosso@chu-Grenoble.fr

CHU GRENOBLE ALPES

UNIVERSITÉ Grenoble Alpes

Purpose: radio-biological indices for dosimetric system assessment

- In radiotherapy the Tumor Control Probability (**TCP**) and Normal Tissues Complication Probability (**NTCP**) are directly **correlated to the delivered doses**.
- The truly delivered dose is *expected* to be as close as possible to the **prescribed dose (PD).**
- Practically, to perform the irradiation, the prescribed dose is translated in **Monitor Units (MU)** by a specific **calculation algorithm** in the TPS.
- However, this algorithm **is changing** from time to time, to improve.
- When the cumulated **clinical experience** for a radiotherapy technique, in one or several departments, is known as **TCP/NTCP statistics**, TCP/NTCP models can be used to assess new dose calculation algorithms and probe the need for an adjustment of the PD and the TCP/NTCP parameters **to keep reproducible clinical results.**

2 Methods

Generation of comparable treatment plans

- **This study was applied to thoracic cancer** (heterogeneity)
- **For each case, 3 treatment plans were generated:**
  - The dose in Plan 1 was calculated with MB
  - The dose in Plan 2 was calculated with AAA
  - *The dose in Plan 3 was calculated with AAA using the same MU from MB in plan 1 as input*
- **Plan 3 calculate the "real" delivered dose with MB and was used to estimate if the prescribed dose should be readjusted when using AAA.**

CHU GRENOBLE ALPES

UNIVERSITÉ Grenoble Alpes

In-silico comparison of treatment plans (1)

- **Dose Volume Histograms (DVHs) data**
  - **Target :** Dmin, Dmean and Dmax, D95%
  - **Lung:** Dmin, Dmean, Dmax, V20 and V30Gy
- **Topographic global dosimetric comparison by 2D Gamma index (γ) [2]**
  - ΔD_{max} : dose difference (%)
  - Δd_{max} : Distance To Agreement (mm)
- **Statistical analysis**
  - **Bootstrap extension of data to define CI of the differences**
  - **Wilcoxon signed rank test:**
    - *p-value* < 5% : statistic significance
  - **Spearman's correlation coefficient :**
    - *r - value > 0.7* : good correlation

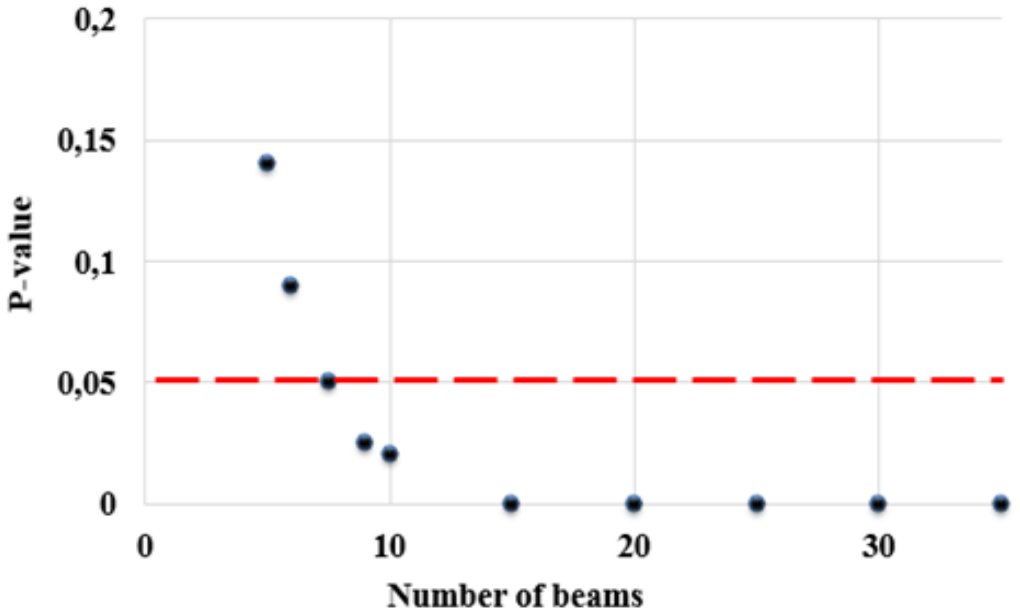
In-silico comparison of treatment plans (2)

- **TCP and NTCP were calculated using Uniform Equivalent Dose (EUD) model [3]**
  - $TCP = 1/1+[TCD_{50}/EUD]^{4.\gamma 50}$
  - $NTCP = 1/1+[TD_{50}/EUD]^{4.\gamma 50}$
  - $EUD = (\sum v_i D^a_i)^{1/a}$
  - v_i is the fractional organ volume receiving a dose D_i and "a" is a tissue specific parameter which describes the volume effect
  - TCD50: the tumor dose to control 50% of the tumors
  - The TD50 is the tolerance dose for 50% complication rate
  - $\gamma 50$ describes the slope of the dose-response curve
- **The set of radiobiological parameters:**
  - TCP for target : a = - 10, $\alpha/\beta = 10$, $TCD_{50} = 51.97$ and $\gamma_{50} = 1.81$ [3,4]
  - NTCP for lung : a = +1, $\alpha/\beta = 3$, $TD_{50} = 24.5$ [5]

3 Results

MU comparison for the same PD (plan 1 vs plan 2)

- **Thanks to Bootstrap estimation** 8 beams would have been sufficient to observe a significant difference between the two algorithms.



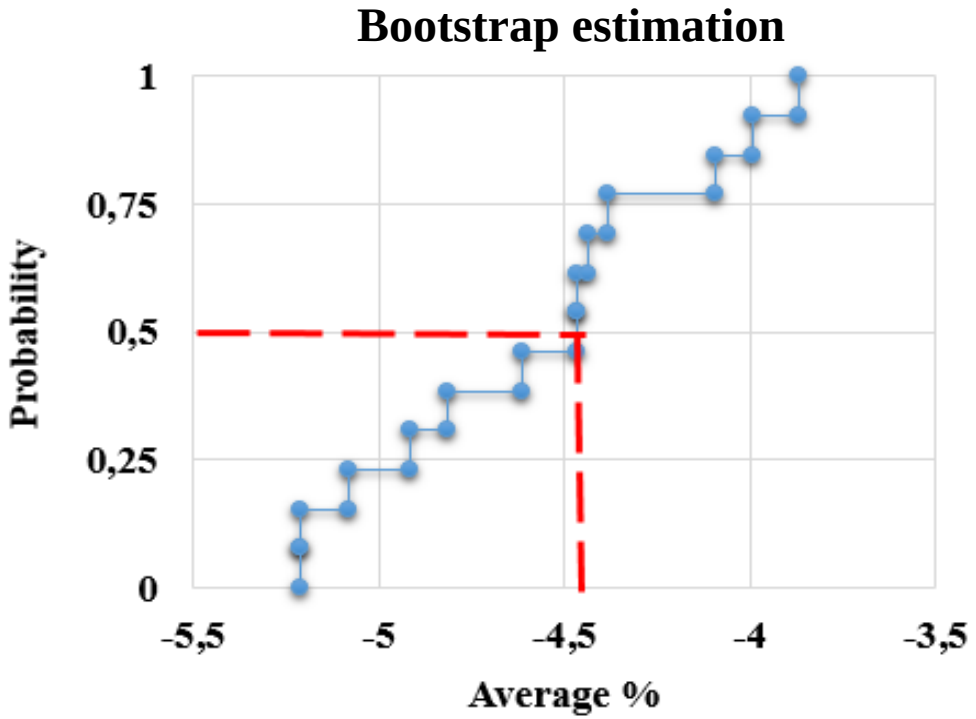
- **AAA** calculates an average of **4.7%** more MUs **CI [+3.9; +5.5]** with $p < 0.001$ and $r > 0.9$

3 Results

Change of "real" delivered dose (plan 2 vs plan 3)

- Comparing plans 2 and 3, shows that the "real" delivered doses when the PD is calculated with MB and the MUs re-calculated with AAA and compared to PD, were reduced by about **- 4.5%** median probability of average, **CI [-5.8; -3.3]**

Let's say: ***"one should apparently prescribed 4.5% less dose with AAA to have the same physical dose delivered than when prescribed with MB"***

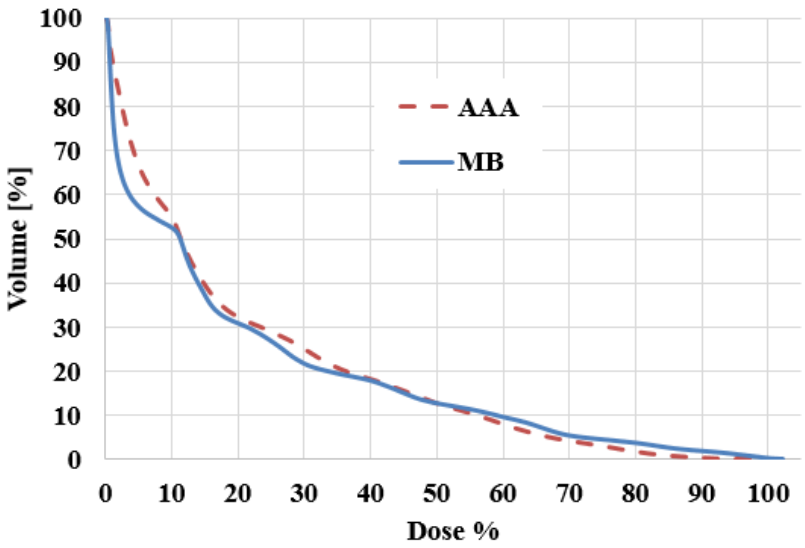


CHU GRENOBLE ALPES — UNIVERSITÉ Grenoble Alpes

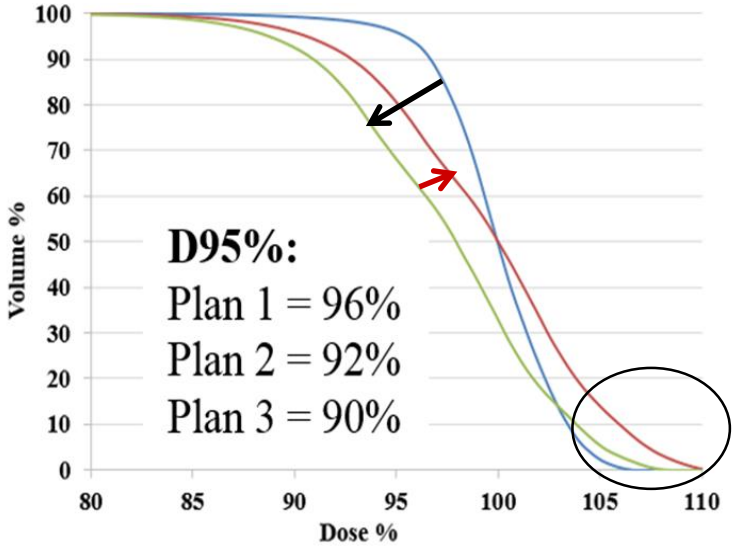
3 Results

DVH metrics and dosimetric data alterations

- **PTV:** the D95% in plans 2 and 3 were significantly reduced with AAA, respectively, **[-5.7; -3.4]** and **[-15.0 ; -10.0]** 95% IC
- **Lung:** the constraint doses V20Gy, V30Gy and mean dose were significantly increased with AAA, 95% IC **[4.1 ; 12.1].**



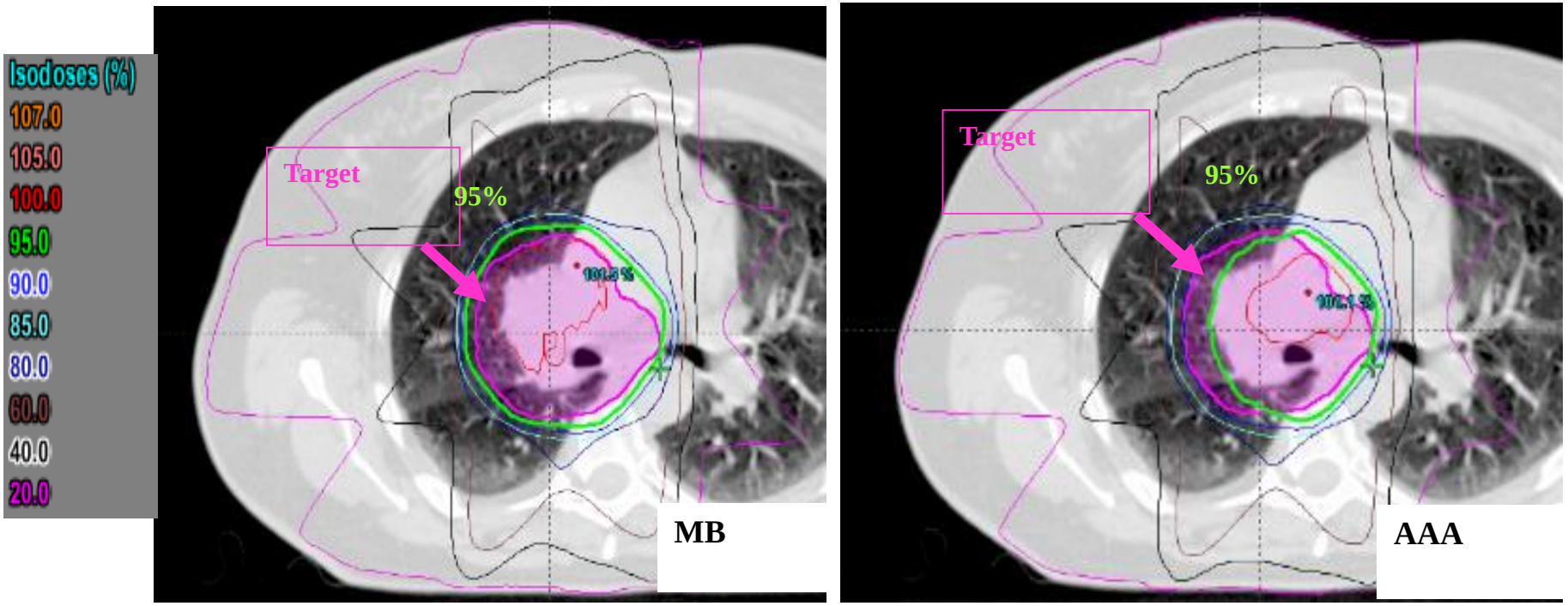
Lung



Target

3 Results

Dose distribution differences: MB vs AAA



Note the large alteration of the 95% isodose (in green)
This is clearly demonstrated by the **2D γ-maps (data not shown).**

3 Results

In-silico study for TCP/NTCP outcome

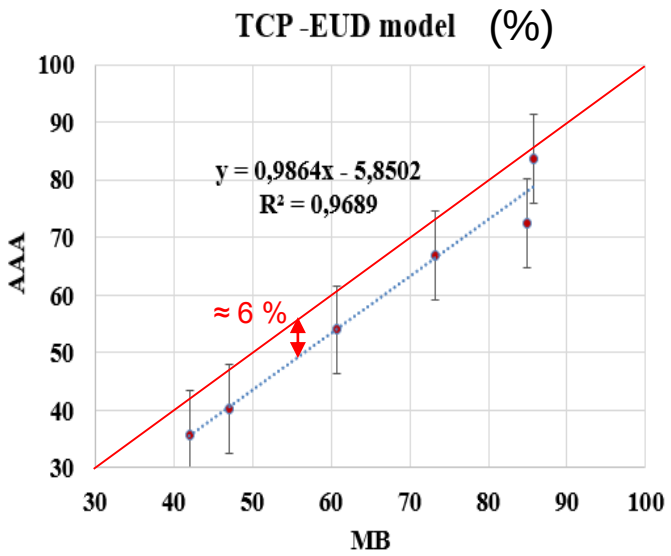
- **TCP / NTCP predictive outcomes based on DVH evaluation (Plan1 *vs* 2):**

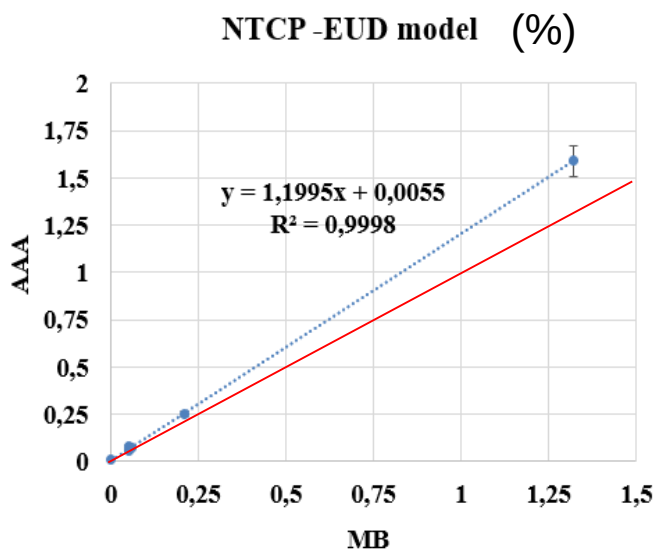
– AAA showed less TCP on average **-12% ± 5SD** relative value (about 6% in absolute value, see figure) with more MUs (!!)

– AAA predicted more NTCP on average **+16% ± 11SD** (*upon a very low value*)

– A significant difference was observed with ($p < 0.01$) in both cases

– A good correlation was observed with a correlation coefficient ($r > 0.9$)





CHU GRENOBLE ALPES — Grenoble Alpes

4 Conclusion

Should the dose prescription be readjusted or optimization pushed on?

- A **significant difference** for dose distribution was observed **in thoracic setting** when using AAA *vs* MB for the same prescribed dose
- Considering AAA is closer to physical reality, the prescribed dose could be readjusted of about -5 % [-3,3 ; -5,8] when changing from MB to AAA but the **optimization should be improved**.
- It could be inappropriate to use the same set of "clinico-radiobiologic parameters" to estimate TCP/NTCP with different dose calculation algorithms.
- Ideally, **the set of "clinico-radiobiologic parameters" should be adjusted to each calculation algorithm** based on the statistics of the real clinical out-come observed in the department of the users.

CHU GRENOBLE ALPES — UNIVERSITÉ Grenoble Alpes

Thank-you for your attention

References

[1]. Chaikh A, Balosso J. Should the dose prescription be readjusted when using tissues density corrections algorithms for radiation oncology?. *J Case Rep Onc Ther 2014; 1(1):01018.*

[2]. Chaikh A, Balosso J, Giraud JY. A 3D quantitative evaluation for assessing the changes of Treatment Planning System and irradiation techniques in radiotherapy. Int J Cancer Ther Oncol 2014; 2(3):02033.

[3]. Niemierko A. Reporting and analyzing dose distributions: A concept of equivalent uniform dose. Med Phys 1997; 24(1):103–110.

[4]. Okunieff P, Morgan D, Niemierko A, Suit HD. Radiation dose-response of human tumors. Inr. J. Radiation Oncology Biol. Phys. 1995; (32)4: 1227- 1237.

[5]. Emami B, Lyman J, Brown A, Coia L, Goitein M, Munzenrider JE, Shank B, Solin LJ, Wesson M: Tolerance of normal tissue to therapeutic irradiation. Int J Radiat Oncol Biol Phys 1991, 21:109–12.

CHU GRENOBLE ALPES

UNIVERSITÉ Grenoble Alpes