# Big data analysis for setup margin personalization derived from intra-fraction motion: a proof of concept


SGRT Community Annual Meeting

December 1st, 2023

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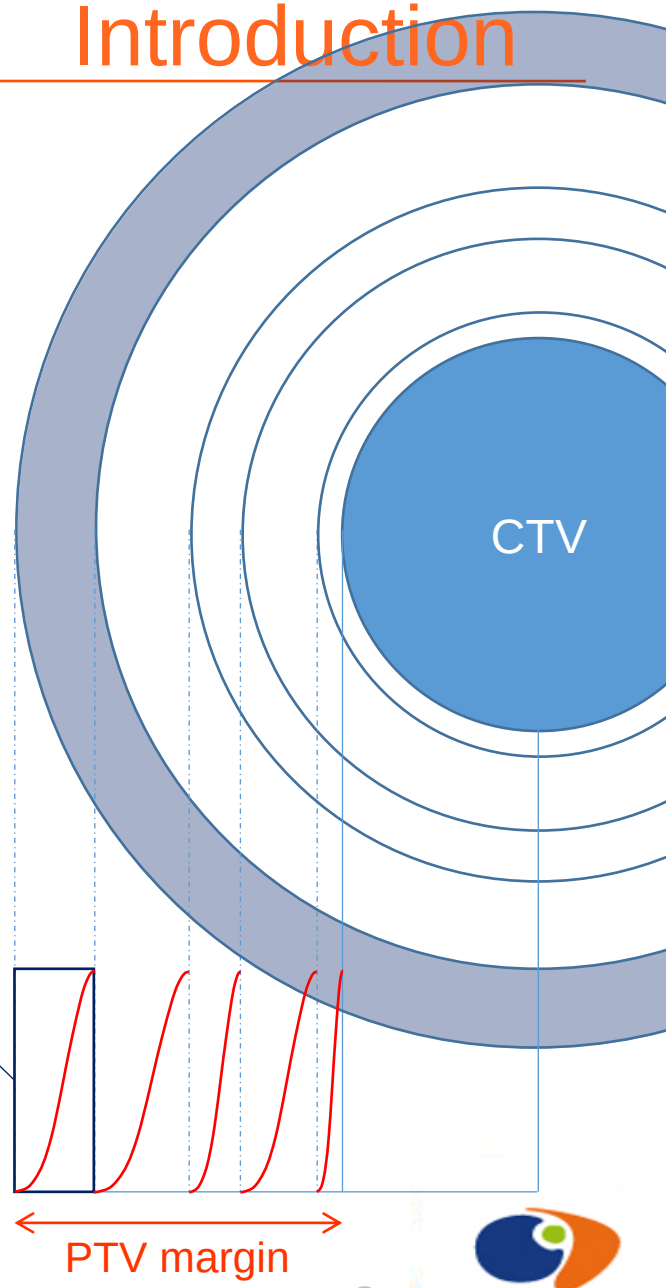
# Introduction

- PTV margin
  - ICRU 50/62
    - Combination of factors
    - Leading to a hypothetical coverage of the CTV
      - *Hypothesis example of Van Herk 2000 : achieve a minimum dose of 95% of the prescribed dose on the CTV for 90% of patients*
  - PTV margin is a sum or combination of different factors
  - ICRU recommendations : Factors have to be evaluated when it's possible
    - By statistical assessment
    - By qualitative assessment when statistics are not applicable
  - All factors are probably can be independently estimated
    - 
  - PTV margin is contained between 0 and the sum of all of the maximum of each independent factors
  - The reduction of PTV margins is a major challenge in the reduction of radiotherapy-related toxicities

TABLE 2.1—*Factors to be considered when defining a planning target volume*

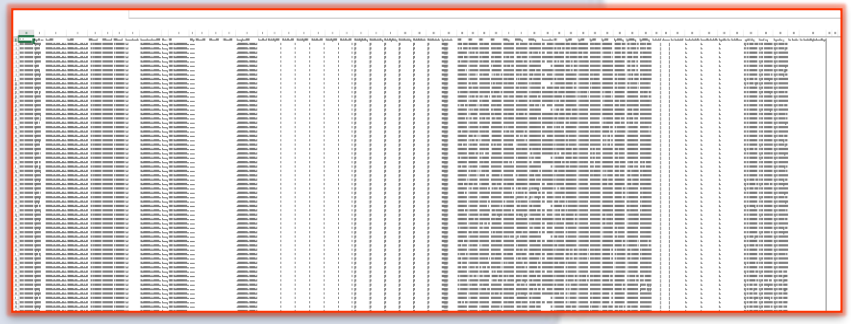
| Category | Intrafractional variations (Variations during a single fraction) | | Interfractional variations (Variations during the entire course of treatment) | |
|---|---|---|---|---|
| | Random | Systematic | Random | Systematic |
| Variations of CTV | | | | |
| In size | Physiological processes (circulation, respiration, peristalsis) | Physiological processes (circulation) | Physiological processes (*e.g.*, degree of bladder filling, bowel gas) | Tumor reduction or swelling |
| In position relative to a fixed point in the patient | Physiological processes (circulation, respiration, peristalsis) | Change in treatment position (prone-supine) | Physiological processes (*e.g.*, degree of filling of cavities) | Weight loss |
| Variations in position of the patient relative to the treatment beams | Patient movements | | Daily set-up | Technical errors |

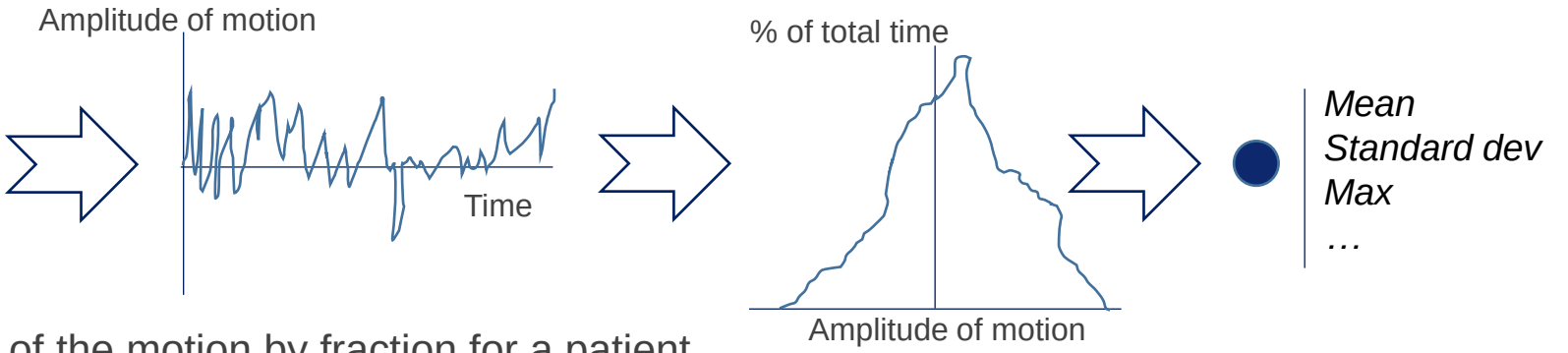
Today PTV margin is standardized by location, dose, ...
From recommendations / guidelines / trials
Most of cases : No patient or machine individualization



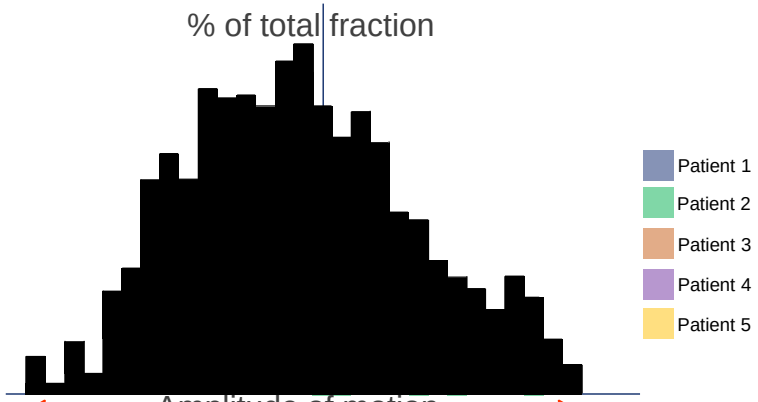
# Introduction

- Surface information
  - AlignRT → Measures intra-fraction external motion
  - Reported in RTD files (translations, rotations, time, … 70 different informations)
  - Data of patient motion available → Amplitude = f(time) → Amplitude histogram → Representative value






  - Histogram of maximal amplitude of the motion by fraction for a patient
  - And for all fraction of all patient
    - → Cumulative histogram
    - → Histogram of the motion for all your patient
    - → Width of the histogram of the maximal intra fraction motion by fraction for all patients = 2 × $PTV_{IFM}$




Amplitude measured for our patients = 2 × $PTV_{IFM}$



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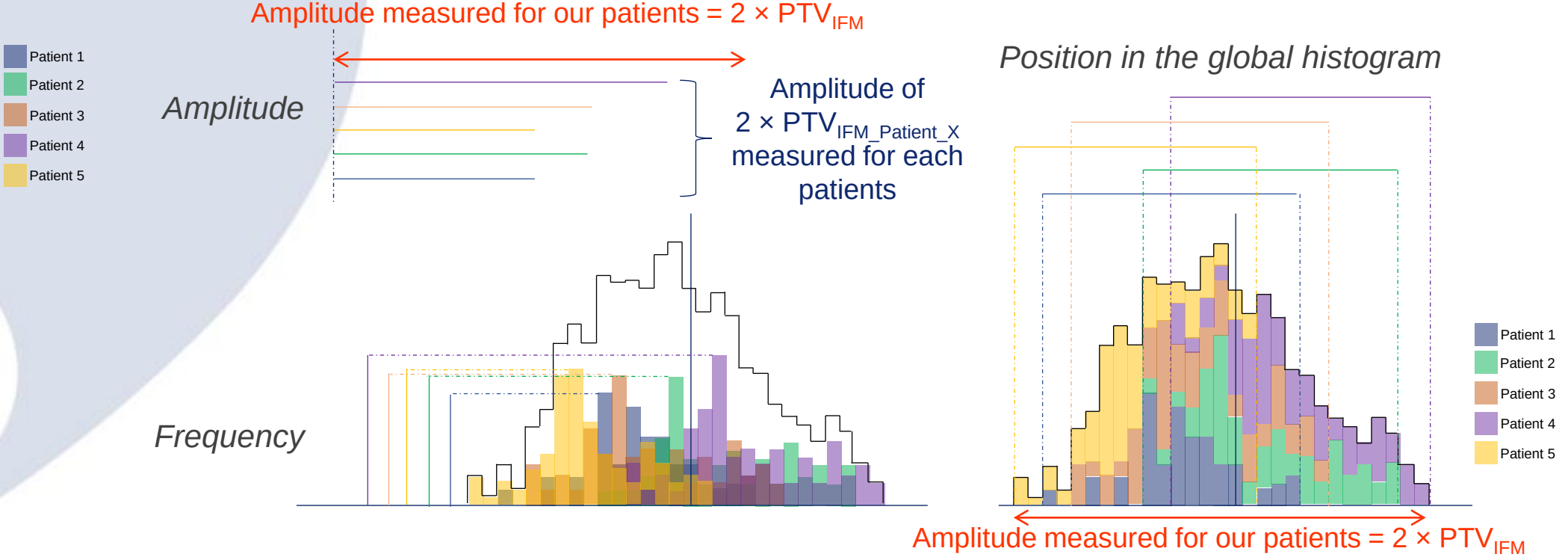
# Introduction

- PTV
  - Width of the histogram of the maximal intra fraction motion by fraction for all patients = 2 × $PTV_{IFM}$
  - Comparison patient by patient
    - Amplitude of maximal motions for a patient is less than the total amplitude

➔ $PTV_{IFM}$ is too large for any patient ? So total PTV margin is too large too ?



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Amplitude measured for our patients = 2 × $PTV_{IFM}$


$$PTV_{Clinical\_Used} = PTV_{AllOtherFactors} + PTV_{IFM}$$

$$PTV_{Real\_Patient\_X} = PTV_{AllOtherFactors} + PTV_{IFM\_Patient\_X}$$

- **BUT** the PTV margins have to be defined before treatment planning

➔ Is it possible to predict theses $PTV_{IFM\_Patient\_X}$ ?

➔ Is it possible to predict patient intra fraction motion ?

➔ Is there a correlation between IFM and clinical / technical data exists ?



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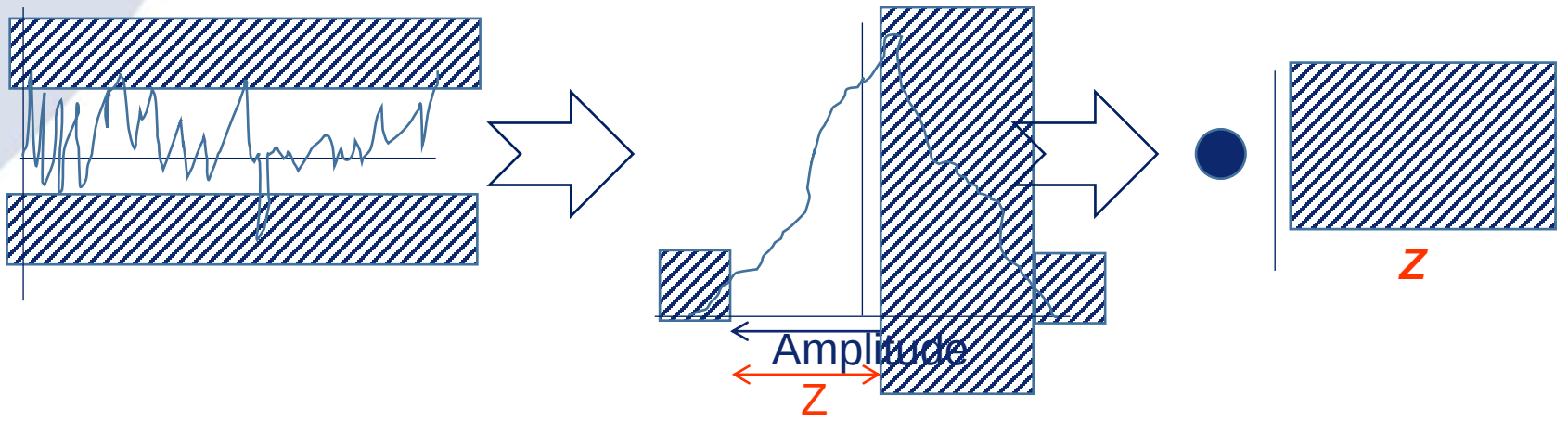
# Method & Materials

- Database
  - 379 patients / 501 plans / 5599 fractions – August 2020 to august 2021 (No lungs or mediastinals / No masks)
    - 50 clinical and technical data → ARIA and Manual extraction
    - AlignRT Measurements → RTD extraction
      - MAG value between the beginning of the 1st beam to the end of the last one
  - PTV hypothesis = The patient have to be in good place for 95% of the time
  - Representative value for each fraction Z define by the Amplitude of IFM for 95% of time divided by 2



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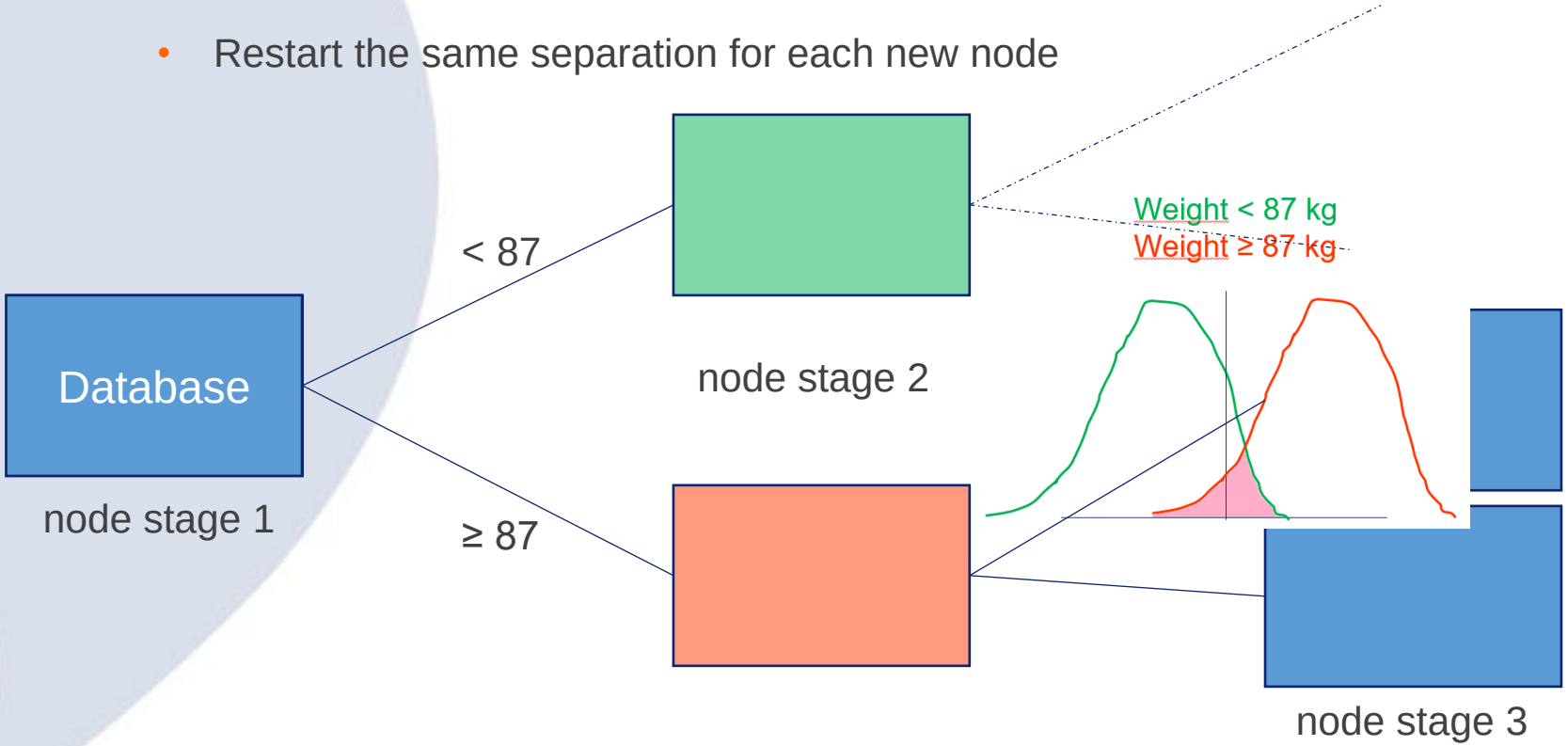
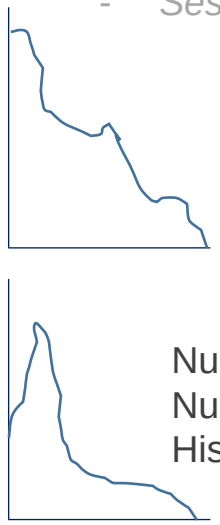
# Method & Materials

- Correlation between clinical/technical and IFM
  - Conditionnal Inference Tree (CIT) : Big data – Machine learning tool
    - Separate the database into the 2 most statistically different parts using only 1 clinical parameter
    - Restart the same separation for each new node




*CIT Configuration :*
- *Library partykit v1.2-16*
- *Level of significance 5%*
- *Node stage limit 5*
- *Session limit by group 100*



Number of sessions
Number of plans = $Np_{node}$
Histogram of Z

- Made for 3 groups of PTV margin : 10 mm; 7-8 mm; 5 mm



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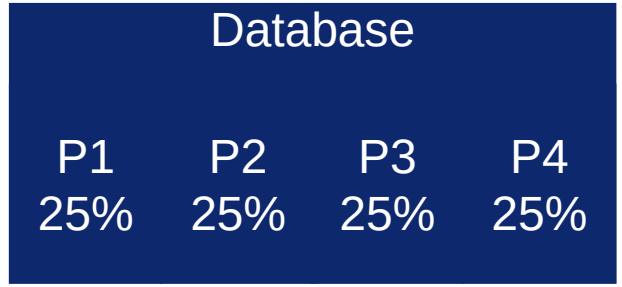
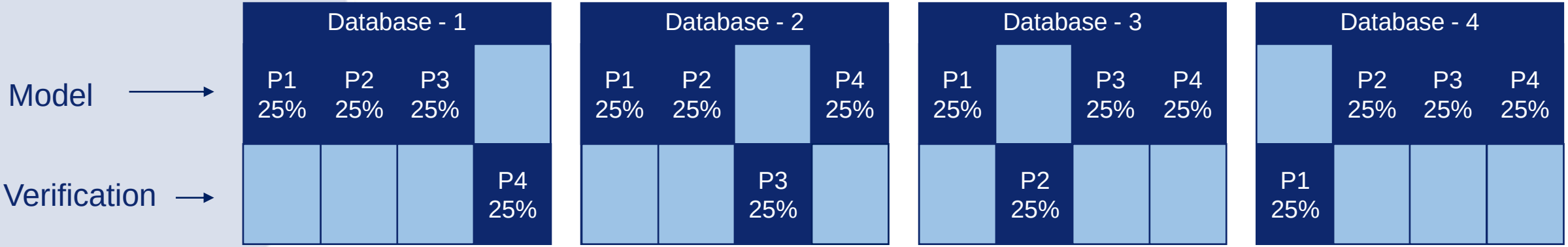
# Method & Materials

- Predictivity test
  - Cross validation : 4 equal parts with random patient/session
    - 4 different models with 75% of the population
    - Model test with the remaining 25% of the population




  - 2 tests with hypothesis of validation :
    - Patient : The patient have a real $Z_{MAX}$ less than or equal to the predicted $Z_{MAX}$ ?
    - Session : The session have a real $Z_{MAX}$ less than or equal to the predicted $Z_{MAX}$ ?



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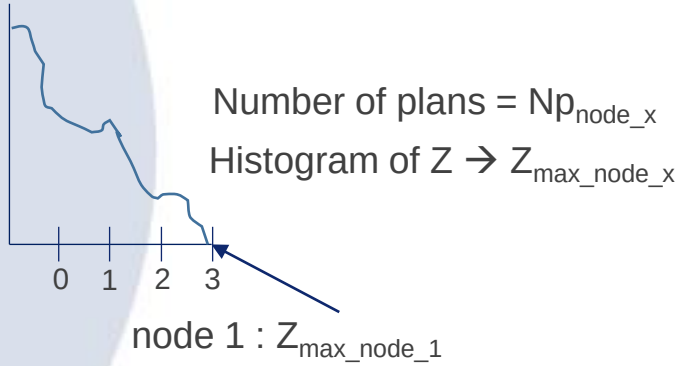
# Method & Materials

- $PTV_{IFM}$ histogram reconstruction
  - For each node, the histogram of Z value have been ranged by millimeter [0;1[, [1;2[, [2;3[, [3;4[, [4;5[, [5;max[.
  - The number of plans for each node have been associated in the range of the maximal value of Z in the node




| $Z_{max}$ | [0;1[ | [1;2[ | [2;3[ | [3;4[ | [4;5[ | [5;max[ |
|---|---|---|---|---|---|---|
| Node 1 | | | $Np_{node\_1}$ | | | |
| … | | | | | | |
| Node x | | | | | $Np_{node\_X}$ | |
| Sum by column | | | | | | |
| Relative | | | | | | |

- $PTV_{Real\_Patient\_X}$ calculation

Standardised PTV margin — Maximal measured IFM for all patient

$$PTV_{Clinical\_Used} = PTV_{AllOtherFactors} + PTV_{IFM}$$

$$PTV_{AllOtherFactors} = PTV_{Clinical\_Used} - PTV_{IFM}$$

$$PTV_{Real\_Patient\_X} = PTV_{AllOtherFactors} + PTV_{IFM\_Patient\_X}$$

Iindividualized PTV margin — Maximal predicted IFM for this patient



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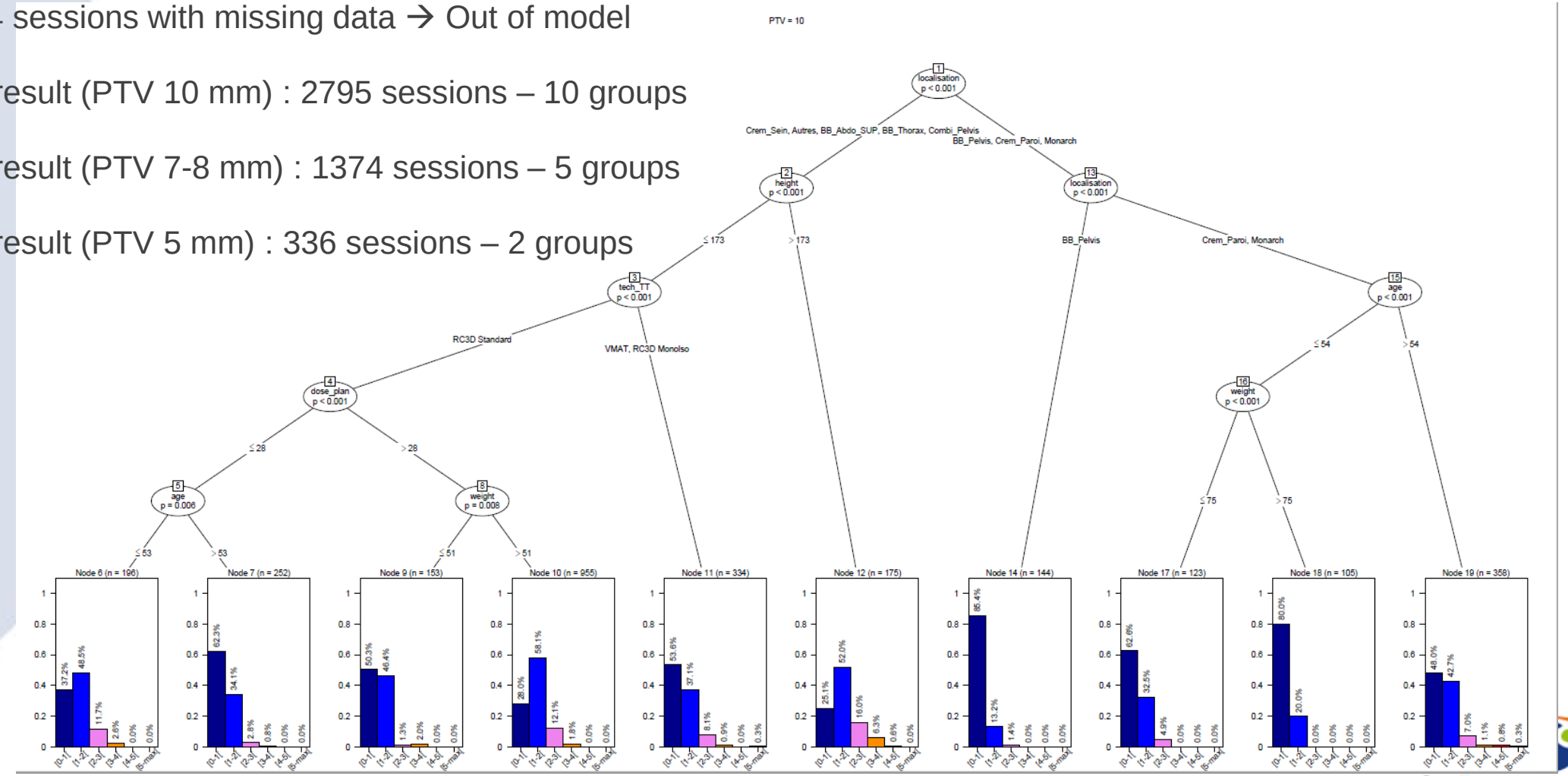
# Results

- Correlation between clinical/technical and IFM
  - 1094 sessions with missing data → Out of model
  - CIT result (PTV 10 mm) : 2795 sessions – 10 groups
  - CIT result (PTV 7-8 mm) : 1374 sessions – 5 groups
  - CIT result (PTV 5 mm) : 336 sessions – 2 groups



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# Results

- Predictivity test
  - Cross validation – Method 1 : Proportion of patient that have a real $Z_{MAX}$ less than or equal to the predicted $Z_{MAX}$ ?

| Cross validation n° | % of true result |
|---|---|
| 1 | 97.8 |
| 2 | 98.4 |
| 3 | 98.9 |
| 4 | 98.3 |

(mean ± std) : (98.4 ± 0.5)%

  - Cross validation – Method 2 : Proportion of session that have a real $Z_{MAX}$ less than or equal to the predicted $Z_{MAX}$ ?

| Cross validation n° | % of true result |
|---|---|
| 1 | 83.9 |
| 2 | 82.6 |
| 3 | 83.3 |
| 4 | 81.1 |

(mean ± std) : (82.7 ± 0.5)%



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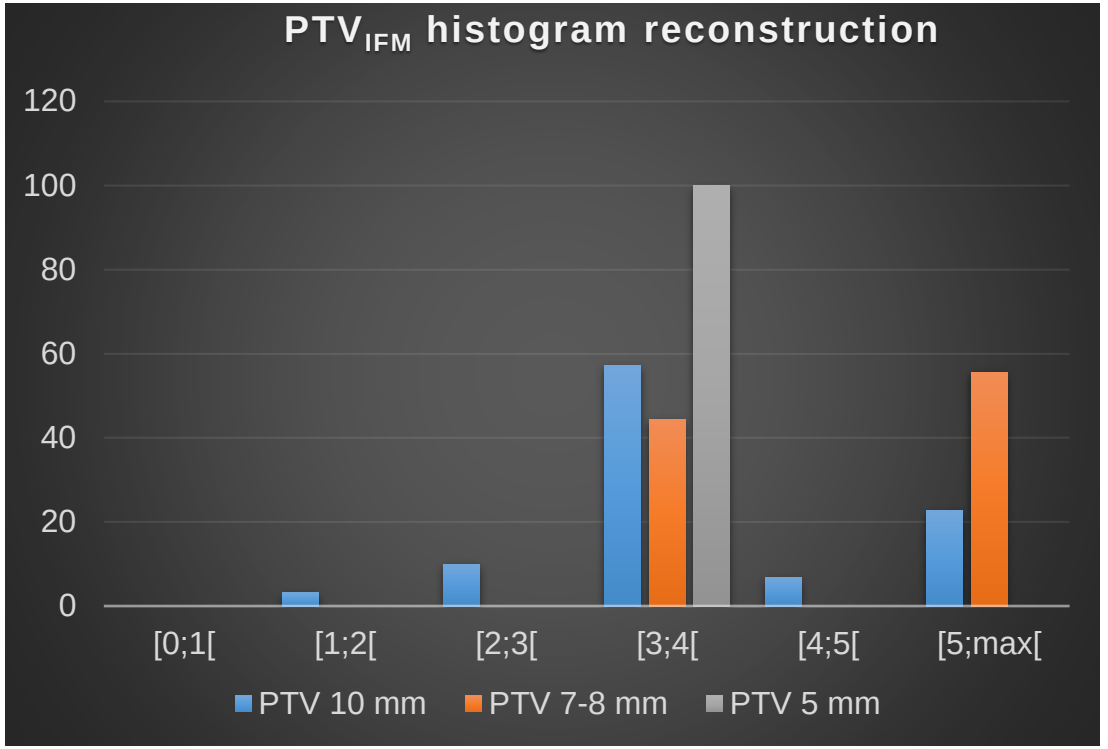
# Results

- $PTV_{IFM}$ histogram reconstruction

| node | N_plans | [0-1[ | [1-2[ | [2-3[ | [3-4[ | [4-5[ | [5-max[ |
|---|---|---|---|---|---|---|---|
| 10 | 62 | | | | 62 | | |
| 11 | 25 | | | | | | 25 |
| 12 | 17 | | | | | 17 | |
| 14 | 14 | | | 14 | | | |
| 17 | 11 | | | 11 | | | |
| 18 | 8 | | 8 | | | | |
| 19 | 32 | | | | | | 32 |
| 6 | 29 | | | | 29 | | |
| 7 | 41 | | | | 41 | | |
| 9 | 11 | | | | 11 | | |
| 0 | 0 | | | | | | |
| 0 | 0 | | | | | | |
| Somme plan par catégorie | Absolu | 0 | 8 | 25 | 143 | 17 | 57 |
| | Relatif | 0,0% | 3,2% | 10,0% | 57,2% | 6,8% | 22,8% |




- $PTV_{Real\_Patient\_X}$ calculation
  - 5 mm PTV margin : can't be individualized
  - 7-8 mm PTV margin : 55.6% of margins can't be individualized but 44.4% can have a reduction of 2.2 mm
  - 10 mm PTV margin : Margin individualisation usefull for 77.2% of patient.

| PTV 10 mm | [0;1[ | [1;2[ | [2;3[ | [3;4[ | [4;5[ | [5;max[ |
|---|---|---|---|---|---|---|
| % of patient | 0.0 | 3.2 | 10.0 | 57.2 | 6.8 | 22.8 |
| Possible PTV individualized (mm) | 5.22 | 6.22 | 7.22 | 8.22 | 9.22 | 10 |
| Possible PTV win (mm) | 4.78 | 3.78 | 2.78 | 1.78 | 0.78 | 0 |



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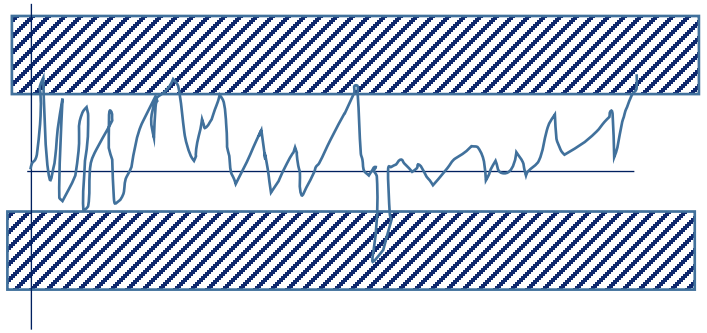
# Discussion

- Discussion
  - PTV hypothesis choice : 100% of patient & 95% of time



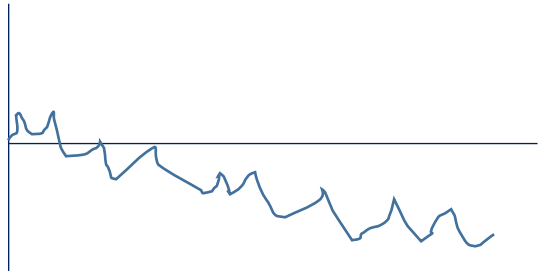
  - Uncertainties combination for PTV margin calculation

$$PTV_{Clinical\_Used} = PTV_{AllOtherFactors} + PTV_{IFM} \ ?$$

  - MAG is the most representative value for PTV ?
    - We have to go to test for combinaison of 3 measured translations

*MAG ? → VRT, LNG, LAT*

  - Z is representative ?
    - Take into account starting position and movement trend



  - CIT algorithm seems to be good but we didn't evaluate others



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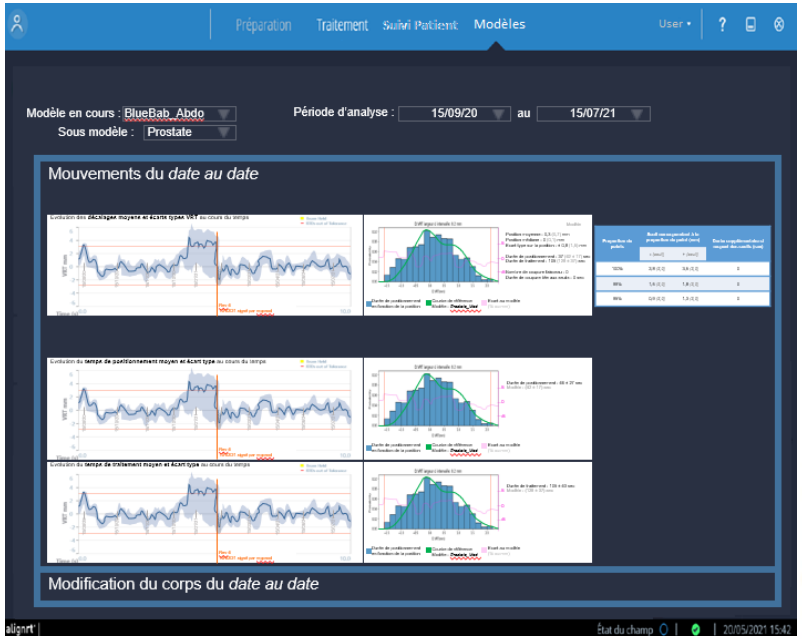
# Conclusion

- Conclusion
  - Correlation between IFM and clinical / technical information exists
  - IFM can be predicted using this correlation
  - PTV margins can be individualized for 62% of our patients on this database
  - Prediction can be verified at each fraction using AlignRT information

➔ Reduction of the toxicities

➔ Verification with a clinical trial ?

- Have to be include in AlignRT ?



*“All truth passes through three stages. - First. it is ridiculed. - Second. it is violently opposed. - Third. it is accepted as being self-evident”*

Apocryphal citation of Arthur Schopenhauer

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## Thank you for your attention

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