**Simultaneous Modelling of PSA in BPH and Cancer Patients Treated by Prostate Surgery**

Alexandre SOSTELLY (1,2), Emilie HENIN (1), Benoit YOU (2), Pascal GIRARD (2) and Mats O. KARLSSON (1)

(1) Department of Pharmaceutical Biosciences, Uppsala University, Sweden
(2) Université Lyon 1, EA3738 CTO, Faculté de Médecine Lyon Sud, Oullins, France

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**Backgrounds and Objectives**

- **Prostate Specific Antigen (PSA):**
  - mainly produced by prostate
  - biomarker for prostate diseases
- **Benign Prostatic Hyperplasia (BPH):**
  - adenoma develops into transition zone [1]
  - treated by transition zone removal (Millin’s adenomectomy)
- **Prostatic adenocarcinoma (cancer):**
  - tumour initially develops into peripheral zone
  - treated by radical prostatectomy [2]

**Aims:** To characterize PSA production from each part of the prostate using a non linear mixed effects model

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**Patients and Methods**

**Patients:**
- 81 BPH patients with a mean of 2.5 PSA assays
- 68 cancer patients with a mean of 9 PSA assays

Patients demographics are similar in the two cohorts

**Methods:**

- **PSA baseline estimation:**
  - No preoperative PSA concentration was available
  - Prostate zone volumes were assessed after surgery
  - Basal PSA values were resulting from the contribution of each zone as a function of corresponding volumes
- **Missing prostate volumes:**
  - Prostate volumes were not reported in 20% of patients
  - Measured volumes were taken for patients where such a measurement was performed and treated as covariates
  - Estimation of missing volumes from the observed volume distribution
- **Censored PSA values:**
  - 33% of PSA values were below the limit of quantification
  - M3 method was used to deal with censored values [3]

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**Model Characteristics:**

- Peripheral compartment represents PSA distribution and PSA is eliminated from the plasma compartment with a first order constant
- Different rates of PSA production for peripheral zone, transition zone and cancer zone were estimated
- Linear two-compartment disposition [4]

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### Results

**Table 1: Parameter Estimates**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transition Zone + Adenoma Volume (BPH cohort) (cm³)</td>
<td>109 (53.89)</td>
</tr>
<tr>
<td>Peripheral Zone Volume (cm³)</td>
<td>22.2 (18.37)</td>
</tr>
<tr>
<td>Transition Zone Volume (Cancer cohort) (cm³)</td>
<td>43.8 (41.38)</td>
</tr>
<tr>
<td>Cancer Zone Volume (cm³)</td>
<td>4.29 (1.62)</td>
</tr>
<tr>
<td>K_{in,CA} (ng.cm⁻³.h⁻¹)</td>
<td>0.0433</td>
</tr>
<tr>
<td>K_{in,TZ} (ng.cm⁻³.h⁻¹)</td>
<td>0.0323</td>
</tr>
</tbody>
</table>

Table 1. Parameter Estimates

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**Figure 1:** PSA model

- K_{in,CA}: Production rate from tumour zone
- K_{in,TZ}: Production rate from peripheral zone
- K_{in,PZ}: Production rate from transition zone

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**Figure 2:** Visual Predictive Check (VPC) for observations

Blue area: 90% predictive interval for the median and 95% percentile; red line: 50% and 95th percentile of the distribution

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**Discussion & Perspectives**

Parameter estimation was supported by both datasets. PSA elimination was “directly” observed in cancer patients after surgery (no more PSA production) and PSA production from transition zone was observed in BPH patients after adenomectomy (residual production). This simultaneous approach allows a better estimation of model parameters even with sparse data. Estimated PSA production rates were in accordance with our expectations: K_{in,CA} > K_{in,TZ} > K_{in,PZ}. PSA half life was estimated to 1 hour which is in accordance to the fast PSA elimination in kidneys [5].

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**Conclusion**

PSA production and its interindividual variability was quantified for each zone of the prostate. The originality of PSA model lies in the simultaneous analysis of two cohorts with different prostatic diseases. In the future, PSA model will be useful to assess the quality of prostate surgery and to help the prediction of risk relapse after surgery.

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**References:**