A NATIONWIDE PULMONARY CARCINOID TUMOR COHORT COLLECTED FROM THE FINNISH CLINICAL PATHOLOGY INTEGRATED BIOBANKS

Tiina Vesterinen

September 10, 2019
Disclosure Information

I hereby declare that I have had business or personal interests in the following industrial enterprises since 1 September 2018:

**Name of the enterprise / Nature of the interest**

<table>
<thead>
<tr>
<th>Enterprise</th>
<th>Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>None</td>
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</tbody>
</table>
FINNISH BIOBANKS: NATIONWIDE COHORTS OF RARE DISEASES

- Biobank Act, 09/2013
- 10 biobanks, 6 hospital-integrated
- Broad, informed consent as the primary justification for collecting samples
- Pathway for transferring clinical and research sample collections to a biobank: opt-out procedure
- Major Finnish clinical pathology sample archives have been transferred and are available for research use
  - Millions of tissue samples from ~3 million persons

Population: 5 537 519
FINNISH CANCER REGISTRY (FCR) COLLECTS NATIONWIDE CANCER INCIDENCE DATA

- Operates under the National Institute for Health and Welfare
- Compulsory for institutions and health care professionals since 1961
- The degree of data completeness in lung cancers >97%

- Every Finn has a unique personal identity number:
  → Combining information from different registries is easy

130489 - 1234

dd mm yy
If even, female
If uneven, male
If -, born in the 20th
If A, born in the 21st
EXAMPLE OF A RARE CANCER: PULMONARY CARCINOID (PC) TUMOR

- Rare malignant neuroendocrine neoplasms, 1-2% of all lung cancers
- Histological subtypes typical (TC, 70-90%) and atypical (AC, 10-30%) carcinoid tumor, classification based on presence of necrosis and number of mitoses
- Primary treatment surgery, no standard treatment for metastasized disease
- TCs rarely metastasize, 5-yrs survival >90%
- ACs more aggressive, 5-yrs survival 40-70%
- Large cohorts needed to study the characteristics of the PC tumors
AIMS

• To explore, how the number of tumors found in the biobanks corresponds to the number of tumors registered in the Finnish Cancer Registry
• To study the bottlenecks of the sample and data delivery process
• How the diagnostic group (TC or AC) of tumors changes after re-evaluation
• To study prognostic factors of PC tumor patients
A 10-year period: 2002-2011

- FCR: 256 tumors, 91% histologically confirmed
- 88% of the expected tumors found in the biobanks
- 63% delivered to us
- 12 tumors excluded
  - Incompatible morphology
  - Not primary PCs but metastases
  - No follow-up data
- 117 (57%) tumors included

### PERFORMANCE OF THE BIOBANKS

<table>
<thead>
<tr>
<th>Hospital region</th>
<th>Local biobank(s)</th>
<th>FCR all</th>
<th>FCR hist.</th>
<th>Number of tumors found in the biobank</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(n)</td>
<td>(n)</td>
<td>orig. (n)</td>
</tr>
<tr>
<td>Helsinki</td>
<td>Helsinki Biobank</td>
<td>93</td>
<td>85</td>
<td>72</td>
</tr>
<tr>
<td>Turku</td>
<td>Auria Biobank</td>
<td>46</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>Tampere</td>
<td>Finnish Clinical Biobank Tampere</td>
<td>60</td>
<td>54</td>
<td>26</td>
</tr>
<tr>
<td>Kuopio</td>
<td>Biobank of Eastern Finland &amp; Central Finland Biobank</td>
<td>34</td>
<td>30</td>
<td>34</td>
</tr>
<tr>
<td>Oulu</td>
<td>Northern Finland Biobank Borealis</td>
<td>23</td>
<td>22</td>
<td>32</td>
</tr>
<tr>
<td>All</td>
<td></td>
<td>256</td>
<td>233</td>
<td>206</td>
</tr>
</tbody>
</table>

We proposed from the biobanks:

Primary resected PC tumor sample + patient follow-up and survival data
206 TUMORS FOUND FROM BIOBANK DATABASES BUT ONLY 129 (63%) DELIVERED – WHY?

1. Sample not found in the biobank archives
   • Tissue samples from 3 million Finns were transferred into biobanks based on registry information, no physical checking of sample availability
   • Prior active research use, no diligent follow-up of sample usage before the biobanking era

2. Lack of tissue material
   • Samples collected primarily for diagnostic purposes can be used for research purposes only if possible future patient care is not jeopardized. Scarce samples were excluded by the biobanks.

3. Incorrect primary diagnoses: pathologist in the biobank scanning the cases excluded these tumors

4. Biopsy samples: unsuitable for our study

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BOTTLENECKS IN SAMPLE AND DATA DELIVERY

1. Sample and data distribution process slow: 6-22 months
   - Our proposals 12/2016 – 9/2018 among the first ones, all processes not optimized yet

2. Challenges in collecting the clinical follow-up data from the patient records
   - Mainly in electronic form: not structured but freely written text
   - Technical skills needed for patient data mining
   - Special medical knowledge needed for accurate patient data mining
STRENGTHS OF THE FINNISH BIOBANKS

- 88% of the tumors were found from the sample registries
- Every Finn has a unique personal identity number: combining biological samples with data from multiple national or local health registers is straightforward
  - survival data from the Population Register Centre
  - cause of death data from Statistics Finland
- Excellent facilities and technical skills for processing FFPE tissue into e.g. TMA format
RE-EVALUATION OF THE TUMORS

- A 20-year period
- Morphology + IHC (Chrom A, SYP, pan-CK, Ki-67), WHO 2015 classification

- 21% of the original diagnoses changed
  - 31 TC → AC
  - 16 AC → TC

Primary biobank database diagnosis

<table>
<thead>
<tr>
<th>Primary biobank database diagnosis</th>
<th>Diagnosis after re-evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC</td>
<td>AC</td>
</tr>
<tr>
<td>n=27 (12.0%)</td>
<td>n=42 (18.4%)</td>
</tr>
<tr>
<td>TC</td>
<td>TC</td>
</tr>
<tr>
<td>n=196 (87.5%)</td>
<td>n=186 (81.6%)</td>
</tr>
<tr>
<td>NE CA</td>
<td>NE CA</td>
</tr>
<tr>
<td>n=1 (0.5%)</td>
<td>n=1 (0.5%)</td>
</tr>
</tbody>
</table>

= changed diagnosis

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CONCLUSIONS

• The Finnish biobank infrastructure offers excellent opportunities for biomedical tissue-based research.

• To be able to develop the biobank operations further, involving more medical knowledge in the sample and data acquisition process is a necessity.

• When working with tissue samples collected over the decades, histological expertise is needed for re-evaluation of the samples.
Performance of Finnish biobanks in nationwide pulmonary carcinoid tumour research

Tiina Vesterinen¹,², Kaisa Salmenkivi¹, Harri Mustonen³, Teijo Kuoppio⁴,⁵, Elisa Lappi-Blanco⁶, Timo Paavonen⁷, Paula Vainio⁸, Aija Knuutila⁹, Olli Carpén¹,¹⁰, Caj Haglund³,¹¹, Johanna Arola¹

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- Paula Vainio
- Teijo Kuopio
- Timo Paavonen
- Olli Carpén
- Elisa Lappi-Blanco

Clinician:
- Aija Knuuttila

Statistician:
- Harri Mustonen

Technical assistance:
- Eija Heiliö
- Jenni Niinimäki

Supervisors:
- Johanna Arola
- Caj Haglund

Biobanks and PC patients

Clinician: Olli Carpén
Clinician: Elisa Lappi-Blanco
Clinician: Teijo Kuopio
Clinician: Tiina Vesterinen
Clinician: Johanna Arola
Clinician: Caj Haglund

Funding: HUS
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Contact: tiina.vesterinen@helsinki.fi