**TBIcare** - Evidence based Diagnostic and Treatment Planning Solution for Traumatic Brain Injuries
Traumatic Brain Injury (TBI) - Facts

• TBI is the most common cause of permanent disability in people under the age of 40 years
• In developed countries, TBI causes more loss of productive life years than cancer, cerebrovascular diseases, and HIV/AIDS combined
• The yearly costs from TBI in Europe exceed 100 billion euros
• There is a steep increase in the incidence of TBIs, with an increase of 21 % over the last five years
• Until now, TBI has been seriously underrepresented in medical R&D efforts
TBI Diagnosis and Treatment - Challenges

• Especially in subjects with multitrauma and inebriation reliable methods to detect or exclude mild (or even more severe) TBI are very poorly developed
• There is a huge inter-individual variability in injured subjects
• Temporal evolution of variable injury mechanisms and pathophysiological heterogeneity across the injured brain make it difficult to predict response to individual treatments
• Treatments are variable and based on poor or lacking evidence
• An extremely heterogeneous injury - “our most complex disease in our most complex organ”
“Our most complex disease in our most complex organ”

Individual variability
- Age
- Gender
- Cognitive reserve
- Education
- Previous TBIs
- Pre-injury health
- Genetic properties...

Injury variability
- Mechanism
- Haematomas
- Contusions
- Axonal injury
- Oedema
- Concomitant injuries
- Intracranial pressure
- Neuroinflammation
- Apoptosis
- Exitotoxicity...

How should I treat???

Treatment variability
- Treatment delays
- Surgical measures
- Cerebral blood flow maintenance
- Seizure detection and treatment
- ICP treatment
- Rehabilitation...

Outcome

This project is partially funded by the European Commission under the 7th Framework Programme (FP7-270259-TBICare)
Complexity in practice…

- Gross pathology may include **axonal injury**, **oedema**, **contusions**, **epidural haematoma**, **subdural haematoma** and **tSAH** alone or in various combinations
  
  \[2^6 = 64\] different types of injuries – simply by gross pathology

- If the order of temporal evolution is considered, the number of combinations is \(6! = 720\)

- Currently we know about 100 variables which are known or suspected to affect the outcome. Many of them are not dichotomous, but simply with alternatives yes/no we have \(2^{100}\) combinations

\[= 1267650600228229401496703205376\]

- **How can we ever reach evidence-based medicine in treating individual subjects with TBI?**

Never, but we can approach it…
TBIcare as a solution

The idea:
• To combine modern statistical methods and system simulation modeling, and
• Data mining methodology, and
• Modern automatic tools to quantify heterogenous physiological data, and
• Large databases with clinical TBI data (including outcome)

➔ To produce a software tool which is able to:
1. Give an accurate estimate about the nature of the injury (= improved diagnostics)
2. Assist in selecting the most appropriate treatment for this particular patients (= improved care)
TBIcare – Objectives

• TBIcare provides an objective and evidence-based solution for the management of traumatic brain injury (TBI) by improving diagnostics and treatment decisions for an individual patient.

• In reaching its goals, the project will provide:
  – improved differential diagnostics,
  – tools to select the best individual treatment and
  – improved prediction of outcome

  by relying on the extraction and combination of a versatile set of physiological observations from a patient using state-of-the-art data mining techniques.

• Using simulation modelling, TBIcare will transfer the scientific Virtual Physiological Human (VPH) concepts to daily clinical practice.
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**Project implementation**

- **Imaging data**
- **Electrophysiological data**
- **Molecular data**
- **Clinical tests**
- **Data quantification**
- **Vital signs**
- **Demographic data**
- **Statistical models for diagnostics**
- **Simulation models for treatment**
- **Software implementation**
- **Optimised diagnostics**
- **Optimised treatment planning**

**Partners:**
- VTT (FIN), GE Healthcare Ltd. (UK),
- Turku University Central Hospital (FIN),
- University of Cambridge (UK), Imperial College London (UK),
- Complexio (FRA), Kaunas University of Technology (LT),
- GE Healthcare Finland Oy (FIN)

**Feb 2011 – Jan 2014**
**Budget 4.2 M€, EC contribution 3.2 M€**

**more info:** [www.tbicare.eu](http://www.tbicare.eu) or [Mark.vanGils@vtt.fi](mailto:Mark.vanGils@vtt.fi)
Data used for modelling and validation

The following datasets will be used for modelling of TBI-related clinical data:

<table>
<thead>
<tr>
<th>Dataset</th>
<th>Size</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMPACT-database (<a href="http://www.tbi-impact.org">www.tbi-impact.org</a>) (global)</td>
<td>11 235</td>
<td>Mostly severe</td>
</tr>
<tr>
<td>University of Cambridge, prospective (UK)</td>
<td>400</td>
<td>Mostly severe</td>
</tr>
<tr>
<td>Turku University Hospital, retrospective (Finland)</td>
<td>&gt; 1000</td>
<td>All severities</td>
</tr>
<tr>
<td>TBIcare prospective* (UK + Finland)</td>
<td>400</td>
<td>All severities</td>
</tr>
<tr>
<td>Tampere University Hospital (Finland)</td>
<td>76</td>
<td>Mild</td>
</tr>
<tr>
<td>TRACK-TBI (USA)</td>
<td>650</td>
<td>Any severity</td>
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</table>

* From University of Cambridge and Turku University Hospital, incl. detailed clinical data + blood biomarkers + acute and late MRI + multifactorial outcome
## Data to be used, different modalities

EIS = electric impedance spectroscopy, ICP = intracranial pressure, Met = metabolomics data, Gene = Genetics data, Clin = Clinical data (injury mechanisms), NTest = Neurological test data.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Type</th>
<th>TBI/CTRL</th>
<th>MRI</th>
<th>CT</th>
<th>PET</th>
<th>EEG</th>
<th>EIS</th>
<th>ICP</th>
<th>Met</th>
<th>Gene</th>
<th>Clin</th>
<th>NTest</th>
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<tr>
<td>TUCH</td>
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<td>800</td>
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<td>-</td>
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<tr>
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<td>Retr</td>
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<td>-</td>
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<tr>
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<td>60</td>
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<tr>
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<td>-</td>
<td>100</td>
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<tr>
<td>IMPACT</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>40000</td>
<td>40000</td>
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Validation and user trials

• Diagnostic tool will be validated using multiple retrospective and prospective datasets, and the process of diagnostic work-up is divided into clinically logical components

• Treatment planning tool will be validated prospectively evaluating the treatment algorithms for different clinical decision-making situations against clinical expertise

• User trials focus on the clinical usability as a diagnostic and decision-making aid in everyday clinical practice
Data Quantification Methods

Global metabolomics and lipidomics & Gene expression analysis: Search new metabolomics, lipidomics and genetics biomarkers related to TBIs

EEG measurements and analysis: obtain relevant EEG features as input for care decision making; methods for detection of epileptic seizures and other adverse events

EIS measurements and analysis: investigate the potential of a novel technology based on electric impedance spectroscopy (EIS) to rapidly reveal structural changes in TBI

Prospective assessment of innovative non-invasive absolute ICP value meter: hardware and software solutions for fast, accurate and reliable non-invasive absolute ICP measurements for early diagnosing of TBI
TBICare: Image Quantification

Structural Networks

Functional Networks

This project is partially funded by the European Commission under the 7th Framework Programme (FP7-270259-TBICare)
Model and software development

Modeling and software development has two main objectives:
• develop a statistical model that predicts the outcome from heterogeneous patient measurements and biomarkers and
• implement the model in a software tool meeting clinical requirements in the care of traumatic brain injuries and
• develop a socio-economic simulation model for understanding interconnections of different aspects in traumatic brain injuries.
Usability

The software tool is specified iteratively via co-development using platform for collaborative interaction between clinicians and information technologists.

TBIcare Tool prototype 1: proposed features for background information, intelligent data entry, and prognostic outputs.
Dissemination - Interactions

• **Dissemination within EU Commission R&TD activities:**
  – Cooperation with Commission – dissemination via EU supported R&D initiatives,
  – Possibilities for co-operating with other EU-funded projects will be followed up.
  – Dissemination activities reported to the Commission as specified in Article II.30.

• **International networking through the collaboration**
  – International structures such as for example centres of excellence in the area of TBI research (the FinBIRD initiative, UK NCCnet and NICE TBI GDG, CENTER-TBI, INCF, IMPACT, TRACK-TBI)
  – EU image and signal processing research resources.

• **Connections with European clinical and medical institutions**

• **Research connections outside Europe**
  – National (USA) and International Neurotrauma Societies, NIH/NINDS CDE

• **Workshops, focus group discussions**

• **Collaboration with third parties (with appropriate NDAs)**

• **General public:** [www.tbicare.eu](http://www.tbicare.eu), [twitter.com/tbiccare](http://twitter.com/tbiccare), e-Newsletter (TBD), youtube (TBD)
Impact of TBICare

- **For healthcare professionals** - optimizes the treatment process, and increases medical knowledge, aids in everyday diagnostics and treatment planning
- **For the patients and their nearest** - minimizes the burden of the injury, it increases quality adjusted life years;
- **For society** - brings reduction in healthcare costs, minimizes losses of productive life years, and
- **For the European industry** - it gives an impetus to increased global competitiveness by providing immediately exploitable innovative methods.

- TBICare is expected to create initial models for common injury types
- Wider clinical usability and reliability requires continuous input of validated clinical data
- The future of TBI medicine is based on an organized system of observational medicine
The TBIcare consortium

<table>
<thead>
<tr>
<th>Participant organisation name</th>
<th>Part. short name</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTT Technical Research Centre of Finland</td>
<td>VTT</td>
<td>Finland</td>
</tr>
<tr>
<td>GE Healthcare Limited</td>
<td>GEHC</td>
<td>UK</td>
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<td>TUCH</td>
<td>Finland</td>
</tr>
<tr>
<td>The Chancellor, Masters and Scholars of the University of Cambridge</td>
<td>UCA</td>
<td>UK</td>
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