BRAIN
TECHNOLOGY
INSTITUTE

POLICY PLAN 2017 - 2020

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Policy Plan BTI

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January 2017

I. Introduction

This document contains the policy plan of Stichting Brain Technology Institute ('BTI') for 2017-2020.

BTI was founded and registered by notary public in Amsterdam on December 14, 2012. The initial reason to establish BTI was to maintain the availability of the Elana Surgical Kit for patients with an aneurysm, tumor or other cerebral vascular disease, who have no alternative treatment option available, with a non-occlusive bypass technique. Up until December 2012 this Elana Surgical Kit was being manufactured and sold through the Dutch corporation Elana bv. This 'Elana Surgical Kit' is based on the invention of Prof. C. Tulleken and his desire to help these patients who could previously not be treated. Over the past decade more than 400 lives have been saved with this Elana technique in Europe, the US and Canada and over 100 neurosurgeons have been trained to use this technique. The Elana Surgical Kit is the only available technique to make a bypass in the brain without temporary occlusion of the blood-flow. This significantly diminishes the risk of stroke.

In December 2012 it was decided to transfer Elana bv into a not for profit organization because of the fact that the worldwide number of patients that are eligible to be treated with this technique is very small (less than 100 cases / year). Even though this technique is commercially not relevant, from a social and humanitarian perspective it has a huge impact on the lives of a few patients, since it is a last resort, lifesaving technique. For this reason BTI was founded as parent institute to Elana bv.

Based on the tremendous amount of research that was conducted to develop and certify the Elana surgical kit from bench to bedside, the knowledge of the people involved, the laboratory facilities and the network with renowned vascular neurosurgeons, BTI's mission is to improve the quality of life for people with neurovascular diseases more in general, through scientific research to new and existing neurosurgical products and through education in this field.

On May 3, 2013 BTI received the ANBI (Algemeen Nut Beoogde Instelling) or 'Public Benefit Organization' status from the Dutch tax authorities. The advantage of the ANBI status is the possibility for private and corporate entities to make tax-deductible donations. Also, BTI does not need to pay taxes on gifts and donations. This policy meets the demand of an ANBI non-profit organization.

Four years after the launch of BTI, BTI has defined additional and more detailed goals and plans for the future. With this policy the board of BTI provides further insight in BTI's mission, goals, activities, funding, marketing and governance.

Claartje R.M. Beks-Ypma, LLM
President

January 2017

II. Mission and Objectives

The mission of BTI is to improve the quality of life neurosurgical patients through:
1. (Co-) development of new, scientifically proven, neurosurgical technologies;
2. Drive education in the field of neurosurgery.

Thanks to BTI's close collaboration with the departments of neurosurgery of University Medical Center Utrecht (NL), University Hospital Zurich (CH), Toronto University Health Network (CA) and Lenox Hill Hospital New York (USA) and BTI's facilities and know-how, BTI is able to translate the results of research done in the laboratory to develop new technological products to treat patients.

The statutory objectives of BTI are as follows:

a. To improve the quality of life for people with vascular diseases by maintaining a leading edge in cerebral vascular research and through the development and making available of unique therapies for patients in selected excellence centers;
b. To maintain the production and certification of the current Elana Surgical Kit as well as production and certification of the upgraded version of this device;
c. Clinical Research and Development with respect to improvements of the Elana Surgical Kit as well as regarding other minimal-invasive neurosurgical therapies / products, including publishing scientific publications of such research in renowned medical journals;
d. Generating Intellectual Property rights;
e. Organizing trainings for neurosurgeons / residents, including providing clinical support during Elana surgeries;
f. Providing PhD, fellow and internship programs;
g. Organizing scientific events and workshops for participating neurosurgeons;
h. Other collaboration projects and grants with international partners for research and development of new products in the field of vascular neurosurgery, and everything related to, connected to and for which can be advanced by the foregoing in the widest sense of the word.

BTI does not wish to make any profit.

Our strategy is to keep focusing on the following activities:

1. *Simplifying neurosurgical bypass techniques:*
   Based on our unique experience developing and marketing the Elana Surgical kit, we will continue to improve this technique and work on expanding both the indications as well as the market for the Elana Technique.
2. *Research & Innovation:*
   Next to our R&D in the field of the Elana bypass technique, we continue to conduct research and development in the field of other neurosurgical technologies. This includes (co-) development and research with third parties.
3. *Education:*
   Provide training to neurosurgeons and providing PhD, fellowship and internship programs.

All these activities serve to improve the quality of life of people with neurosurgical diseases by making available new, scientifically proven, neurosurgical devices:

From out-of-the-box thinking to evidence based devices.
Dedicated to improve quality of life.

III. Activities

In order to fulfill our mission and to meet our objectives, BTI conducts the activities as described in the following paragraphs.

1. Simplifying neurosurgical bypass techniques

A. Elana Surgical Kit

The Elana (Excimer Laser Assisted Non-occlusive Anastomosis) technique is a non-occlusive bypass technique for patients with aneurysm, ischemia or tumor who have no safe alternative treatment option available. The Elana Surgical Kit consists of a laser catheter and a platinum ring:

Detailed information on this technique can be found on www.elana.com.

The Elana Surgical Kit is certified as follows:
2005: Europe / CE
2008 Canada / Health Canada
2011: USA / FDA (HDE)

BTI will keep this Elana Surgical Kit available in Europe, Canada and the USA and intends to maintain its certifications, through observation of all legal and regulatory requirements.

On request of surgeons in Brazil BTI is currently in the process to have the Elana Surgical Kit approved by ANVISA in Brazil. This certification process takes place at the expense of the local hospital / distributor and sales of Elana surgical kits will directly benefit the budget of BTI.

B. Clip 3.0

BTI has developed a suture-less clip to make the Elana technique easier and faster and hence safer for the patient. By using this Clip device it is no longer necessary to make sutures deep in the brain in order to make a bypass without temporary occlusion of the blood flow. Through

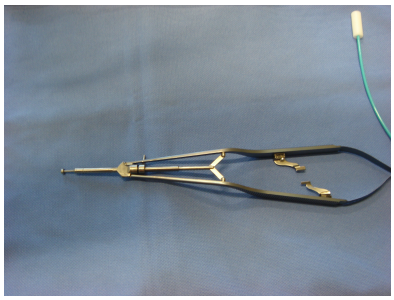
this clip, the bypass procedure will be shortened and simplified, which will benefit the patient. The neurosurgical department of UMC Utrecht has intensively tested this newly developed device in various laboratory settings and it is now ready to be used in a clinical setting. This Elana Clip 3.0 Surgical Kit consists of the following products:

Elana Clip 3.0

Chamber Cone laser catheter

Fixation clip

In order to apply the Clip 3.0 on the recipient artery, a newly developed applier, the Elana Applier, needs to be used:



Elana applier

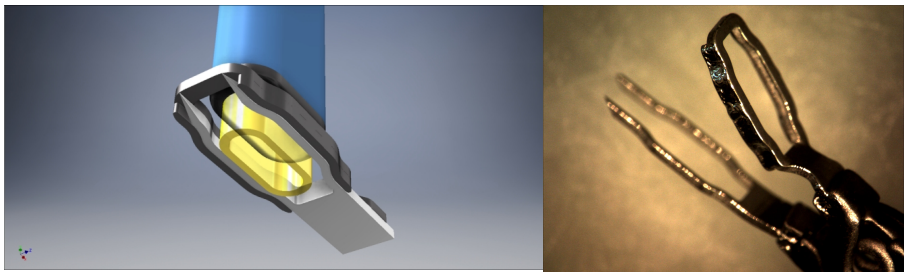
A clinical pilot study at UMC Utrecht for the Elana Clip 3.0 surgical kit started in October 2014. This pilot study includes enrollment of 5 subjects, 3 patients had been enrolled by year-end 2016. Since the patient population for the Elana devices is so small and upon successful conclusion of the clinical pilot study, BTI is planning to make the Clip 3.0 Surgical Kit available to patients in the near future through an international, multi-center, prospective clinical study conducted by highly specialized and trained vascular neurosurgeons.

2. Research & Innovation

Through a unique combination of BTI's (laboratory) facilities, know-how and collaboration with world-leading vascular neurosurgeons, BTI is able to facilitate all steps from idea / invention, to (pre-) clinical research and testing to certification of a product in the neurosurgical space. Herein below is an overview of the current projects and possible future research activities, all-aiming for new technologies, tools and treatment options for neurosurgical patients.

A. Non-occlusive bypass on smaller arteries

The current Elana Surgical Kit and the newly developed Elana Clip can only be used on the large vessels in the brain on patients that can not tolerate a conventional bypass where the blood flow is temporary being occluded. However, there is still a (small) group of patients that is eligible for an Elana bypass, but cannot be treated with this technique because of the fact that the size of their blood vessel where the bypass needs to be placed is too small. Up till today these patients are being treated with a conventional bypass, which creates a relatively high risk of stroke or other serious complications. In collaboration with UMC Utrecht, BTI is now developing and implementing a smaller, oval clip device. Through such a device a new group of patients with an aneurysm, tumor or ischemia can benefit from a safer, non-occlusive sutureless bypass technique. This research program has been made available thanks to a fantastic grant BTI received from Fonds NutsOhra.

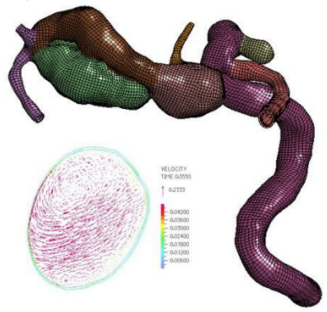


After the initial design of this oval clip and catheter in-vitro bench testing confirmed the mechanical operation. However due to a technical bottleneck, a redesign was necessary to improve the view of the surgeon when implementing the clip. This delay resulted in a budget-

neutral extension of this implementation project until mid 2018 to finalize and analyse all pre-clinical testing.

B. Mathematical Flow Model

This PhD project of Jasper Helthuis, MD is focused on the development of a mathematical model to predict flow in major cerebral arteries. Such a model, for clinical use, of the exact blood flow in the arteries of the brain does not yet exist and will provide insight on e.g. the best location for a bypass in the brain, which can impact / improve the treatment options of patients with different types of cerebrovascular disease. This research takes place in collaboration with UMC Utrecht and the Indian Institute of Technology Madras (IITM) in India. The Dutch and Indian authorities approved a 4-year research grant. The IITM has extensive experience in finite elements analysis, which will be incorporated in this flow model.



The ultimate goal of this project is to have a tool or even an app that can easily be used to predict intracerebral flow based on medical images. Using these predictions it might be possible to say where and how to construct a bypass. It might even be possible to build a product, which says where to place your bypass and how much chance of success the bypass has.

This research project will be finished by October 2018. By that time we hope to continue with our collaboration with India and to improve the (mathematical) flow model that is currently being developed into a clinical, validated, easy to use model.

C. Co-Development of Dural Sealant

The development of the Elana technique has been documented in 35 (!) peer reviewed publications and is a great example of 'bench to bedside' research and of evidence based technology. BTI's goal is to expand such bed-to-bedside research and hence bring evidence based technologies to the bedside, which will benefit the patients.

Due to BTI's facilities, experience, network and know-how, BTI is a great partner for commercial medtech companies to conduct (pre-) clinical research for existing or new neurosurgical medical devices. The data will be published in peer-reviewed journals and may result in evidence-based technologies. This perfectly fits the mission of BTI.

In 2015 BTI started a collaboration with Polyganics B.V. to co-develop a scientifically proven, evidence based, watertight dural sealant to prevent cerebrospinal fluid (CSF) leakage after durotomy (incision of the tough, outer membrane of the brain and spinal cord).

Polyganics develops, manufactures and commercializes innovative bioresorbable medical devices and is developing the dural sealant. At BTI we designed the protocols for the in-vitro and in-vivo experiments, developed adequate in-vitro models and perform all ex-vivo and in-vivo experiments. All data resulting from this research will be published in peer-reviewed journals (just like our other research projects). BTI and Polyganics received a grant from the Netherlands Enterprise Agency for this collaborative research project.

3. Education

A. Annemarie Tulleken Fellowship

BTI will start in 2017-2018 with a fellowship (a 'travelling observer ship') for a highly talented and motivated young neurosurgeon. During this fellowship the neurosurgeon will be able to visit up to four top neurovascular centers in Europe, USA and Canada for maximum 2 weeks per site to observe specialized and complicated cases. BTI believes that such a fellowship will help create a new generation of vascular neurosurgeons that have an interest and the skills to treat a small group of patients with life threatening diseases through state-of-the-art technologies.

B. PhD, fellow and internship Programs

Since the foundation of BTI up till 2016, BTI has provided spots for four PhD students. In the next few years we expect to maintain or extend this number of PhD students.
BTI is also continuously hosting 1 or 2 students as interns of the Life Sciences institute in Utrecht. BTI has also welcomed researchers from the (international) institutes of the BTI board members, med students from Utrecht University as well as students from the Technical University Delft.

C. Courses and workshops

BTI will continue to organize microsurgery / Elana workshops for international neurosurgeons, OR staff etc.

IV. Funding

BTI and its subsidiary Elana bv are currently being funded through the following streams of income:

- **Donations of Participating Centers**

A large part of the revenues) are received through the annual donations of UMC Utrecht (approximately €170.000/year).

- **Subsidies and Grants**

In the past years BTI / Elana received a grant from Fonds NutsOhra and various grants from the Netherlands Enterprise Agency with a total value of approximately €350.000.

- **Collaboration with Medical Device companies**

Through our collaboration with Polyganics B.V. additional funds are being generated. In 2016 proceeds were approximately €135.000.

- **Sales Elana products**

All proceed of the sales of Elana products (clinical and training) are used to fund the activities of BTI. The past few years annual proceeds of approximately €100.000 were generated through the sale of Elana products and services.

- **Donations**

During the past few years BTI received multiple private donations (varying from €10 - €25.000) to support our activities

- **Fundraise Activities**

BTI has conducted various fundraise activities throughout the past years among others the following:

a. BTI@hlon
   In June 2014, BTI hosted a triathlon in Spain, the BTI@hlon to raise funds for BTI.
a. Fundraising Dinner NYC
b. Various Online Art Auctions in collaboration with Catawiki
   These art auctions took place in collaboration with **Catawiki**, the world's leading and fastest growing online auction house for art and exceptional items and collectables. Half of the proceeds of the sale of the art works go to the artist, the other 50% to BTI. Catawiki has very generously waived their seller's commission in these auctions in order to support BTI.

BTI will continue to organize fundraisers. All donations, subsidies, proceeds of Elana Products and fundraise activities are being used to fulfill our mission.

V. Future

For 2017 and beyond, BTI plans to expand its research activities and also its proceeds by extending the co-development activities with Medical Device companies. Polyganics has already indicated their wish to expand and intensify the R&D with BTI which will result in more (1) independent, evidence based technologies that will benefit the lives of people with neurosurgical conditions, (2) scientific output in peer reviewed journals (BTI will submit all results for publication, no matter the outcome, which will safe guard and/or improve the quality of new technologies that are being brought to the bed side); (3) funds to support and expand BTI's own research and education projects.

Next to collaborating with Polyganics, BTI plans to collaborate and co-develop with other MedTech companies which will both serve BTI's mission and goals and will help BTI funding them. Through such an expansion of the research activities, BTI hopes to become less dependent of the donations from the hospitals.

Eventually BTI's ambition is to develop world wide accepted quality benchmarks in new neurosurgical technologies

With regard to funding, BTI also will keep seeking grants and subsidies for research projects and will continue to organize fundraise activities. For example, in 2017 BTI will organize a large fundraising event in the Moco Museum in Amsterdam, with partners such as American_Express and Christies'. Fundraise activities in collaboration with Catawiki will continue in the future.

Furthermore, BTI aims to become a charity organization supported by the 'Vrienden Loterij. This is a Dutch lottery organization that financially supports non-profits in the field of healthcare and wellfare. Since 1998 over €500 million has been donated through this lottery organization. The Vrienden Lotterij is part of the Holding National Charities Lotteries N.V. and supports a limited number of charities through their earnings. By September 30 each year a non-profit can submit a well documented request to become one of their new beneficiaries.

Requirements are:

- Be active in the field of health and/or welfare
- To have broad public support and social approval
- National reach
- Complimentary to existing group of beneficiaries
- Own funding of minimum €400.000
- Professional organization / ANBI status.

BTI plans to submit a request either by September 30, 2017 or 2018.

V. Organization

Details of BTI are as follows:

- Stichting Brain Technology Institute
  Yalelaan 44
  3584 CM Utrecht
  The Netherlands
  Phone: +31 302537276
  Email: info@bt-i.org
- Chamber of Commerce (Kamer van Koophandel) Number 56666748
- RSIN Number 852247448
- BTI has ANBI status

BTI is a non-profit institute organized under the laws of the Netherlands. The board members are:
Claartje Beks-Ypma, LLM (Utrecht, NL), President, Daily board
David Langer, MD (NY, USA),
Prof. Luca Regli, MD (Zurich, CH)
Prof. Gabriel Rinkel, MD (UMC Utrecht, NL)
Prof. Michael Tymianski, MD (Toronto, CA) and
Bart van der Zwan, MD (UMC Utrecht, NL), Daily Board.

BTI's board members do not receive any salary, neither directly nor indirectly.