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Biobanking - an ongoing challenge for
personalised medicine



BRoTHER – a new biobank network in the centre of Europe to promote digitalisation in biobanking

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Summary

Biobanking is a fast-growing field in basic, clinical and translational research. With that, biobanking is crucially involved in the further optimisation of personalised medicine, which is one of the leading concepts in modern medicine. Since personalised medicine works with highly specific and well-characterised cohorts, the interaction of biobanks will become more and more important to enable the setting up of relevant collectives for basic and translational research.

In special characterised entities and in rare diseases, a multicentre approach is crucial to ensure the inclusion of significant numbers of biobank specimens in an appropriate time. Digitalisation and the possibility to share information and knowledge by digitalisation represent an important issue within the networking of different biobanks which are active in the clinical context. The interaction and co-operation of biobanks of different countries must overcome specific challenges even if these countries are located within the European Union.

The project, BRoTHER (Biobank Research on Telemedical Approaches for Human Biobanks in a European Region), is aimed at analysing the obstacles which have to be overcome if clinical related biobanks from two national healthcare systems want to work together and set up common biobank projects by help of digitalisation.

Furthermore, BRoTHER is created to disseminate the idea of biobanking to young academics and to a broader public. The project is supported by a grant of the Bavarian-Czech University Agency (BTHA) with funding coming from the Bavarian State Ministry of Finance.

Biobanking - an ongoing challenge for personalised medicine

Biobanks represent crucial resources for both clinical and basic science. They are closely connected to the development of the concept of personalised medicine. In this context, biobanks are an important prerequisite for all the elements of personalised medicine, which are translational research, new drug development, but also research in prognosis and prediction. In the last two decades, there was a rapid development regarding the number of new biobanks and the dimension of existing ones.

With the growing number of biobanks, the functions, characteristics, the aim of several biobanks and the nature of the biomaterial has changed. Consequently, the definition of a biobank is not a distinct one but is dependent on the function of the biobank and the nature of the stored 'biomaterial'. In this context, it is important to realise that the term 'biomaterial' describes both real biological material such as tissues, cells, DNA, RNA, body fluids or even hairs or parts of the microbiome and virtual 'biomaterials' which are images, clinical data, laboratory values and even many other data (Fig. 1).

The value of a biobank specimen, especially of a real biomaterial such as a tissue specimen, is highly dependent on its biological quality and the potency to combine it reliably with associated clinical and laboratory data and if possible or necessary with several imaging data. Actually, in international consortia, great efforts are made to analyse the influence of the various pre-analytic factors on the biological quality of bio-specimens. This is of special importance since the analytical methods became more and more sensitive and with that, various candidate molecules could be analysed even on the tissue level – if the biological quality and the tissue integrity were preserved properly within the biobank process. With this regard, there was a real change in paradigm within the biobanking scene. Initially, it was believed that high-end analytic methods could compensate a lack of biological quality, but we had to learn that only high-quality biospecimens lead to reliable, high quality analytical results which could be used for high quality clinical or experimental trials. Thus, nowadays a main focus in biobanking is put on biospecimen quality.

The biological quality and integrity of a biospecimen is highly dependent on the pre-analytical conditions from the interventional removal until storing as well as on the storing conditions. Furthermore, taking these new aspects together, one could create a new definition of a biobank specimen – this is a defined biological material, which is obtained processed and stored in a reliable and documented manner and which is combined with valid clinical data. With view to specimen quality, there are three important goals within the biobank community:

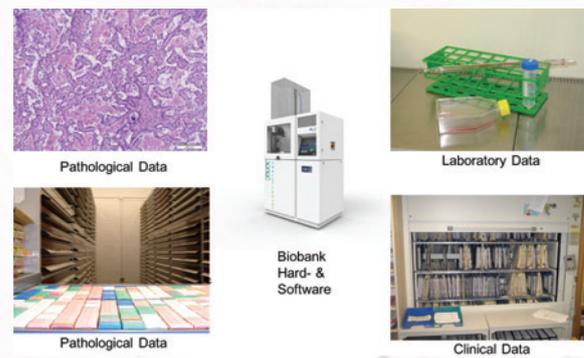


Fig. 1 Our biobank concept follows the philosophy of data rich biobanking. This includes the interconnection of different databases to integrate pathological, clinical and laboratory data in the specimen history.

first to find the best pre-analytical conditions, second to document all pre-analytical processes as well as the storing conditions and third to harmonise the pre-analytical work-flow and the documentations in different biobanks.

Taking into account the variability of biobanks and their environment (as mentioned above) it becomes clear that this is a huge challenge. On the other hand, the harmonisation of biobanks is crucial for building appropriate consortia for clinical and experimental trials in the cadre of the optimisation personalized medicine.

In this context, building networks of biobanks represents a crucial element to enable large multicentre trials, especially in the research of rare diseases. An important pre-requisite for the appropriate exchange of biobank specimens for its potential use in research projects represents the harmonisation of the pre-analytical workflow, the quality control management of the biobank-workflow and the protocols of the analytical methods of the connected biobanks. On the European level the Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium (BBMRI-ERIC) is an important network for biobanks in Europe.

BBMRI is a European leader in biobanking and is crucially involved in further developments of the biobank idea. Within BBMRI and BBMRI-ERIC great efforts were made to harmonise various aspects of biobanking on the European level. In addition, there are several scientific societies bringing scientists from various disciplines together working in the environment of biobanks or repositories respectively. Two well-known Societies are the European, Middle Eastern and African Society for Biopreservation and Biobanking (ESBB) and the International Society for Biological and Environmental Repositories (ISBER). These two societies and even others which may be more specialised on specific topics in the field of biobanking and preservation, illustrates the broad interdisciplinary approach of this field. This also

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Fig. 2 BRoTHER represent a consortium to facilitate the co-operation of Biobanks in Bavaria and the Czech Republic with the aim to engross the relation of these two neighbouring regions. With that purpose BRoTHER became funded by the Bavarian-Czech-Research Agency (BTHA) with money from the Bavarian State Ministry of Finances, Development and Home

illustrates the multidisciplinary facets which are involved in biobanking and which should be considered as important pre-requisites for both the establishment and the conduction of a biobank.

Furthermore, the fact of the existence of several national and international societies and consortia dealing with the different points of biobanking also illustrates the need to bring researchers together in an interdisciplinary manner to enable the exchange and establishment of common structures. These societies and consortia are also important to interact with politics on different levels and with research foundation agencies to discuss and to clear the legal framework for biobanking, to clear the way for research programmes dealing with biobanking and to find possibilities for the sustainability of biobanks.

However, besides these great networks and consortia, regional biobank networks with a smaller number of partners could also give an innovative input in the biobanking idea. Regional biobank networks could focus on the set-up on common projects with biobank specimens or on the harmonisation of workflows in a circumscribed biobank environment. Since regional biobank networks have to harmonise a smaller number of different local workflows, management systems and local regulations, the harmonisation process itself could be monitored easily. From this experience the great consortia might profit from the harmonisation of multiple biobanks.

In this context, we hope that the harmonisation of our new regional biobank network could be finished within an appropriate time so that hopefully we can begin to set up common research projects. Obviously, such regional networks should neither be seen as a template for the interaction of biobanks on the European level nor as a competition of the great European networks. However, one important aim of our regional biobank network is not only to identify various obstacles within the implementation of

harmonisation processes at the member biobanks, but also to monitor the way how harmonisation problems were solved. The monitoring of the harmonisation process and the troubleshooting within our regional network could be inspiration for a greater network. The communication and the exchange with relevant European networks such as BBMRI and BBMRI-ERIC is given by the fact that some of the members of our network play an active role within BBMRI. Furthermore, the German partners are involved in the standardisation process of biobanking both on the national level as members in the German Institute of Normation (DIN) and as member in the International Standardization Organization (ISO).

In addition, the monitoring and troubleshooting of first common projects of BRoTHER could also give valuable information for the European networks. To enable an optimal collaboration of our regional biobank, web-based tools for the data exchange are mandatory to guarantee the long-term success of such a network. In this context, the digitalisation of a smaller biobank network seems to be less complicated. Taking these thoughts together, we are convinced that the regional biobank network will significantly improve the translational and basic research within the connected partners and give interesting information to BBMRI and BBMRI-ERIC.

BRoTHER - regional co-operation for visionary work

BRoTHER represents an international and interdisciplinary consortia project, which was funded by a grant of the Bavarian-Czech Research Agency with financial resources of the Bavarian State Ministry of Finance, Land Development and Homeland with a funding period of three years (Fig. 2).¹

BRoTHER is an acronym standing for: 'Biobank Research on Telemedical Approaches for Human Biobanks in a European Region.' Furthermore, this



Fig. 3 Members of the BRoTHER consortium from left to right: Judita Kinkorova (Pilsen), Christoph Brochhausen (Regensburg), Claudia Fischer (Regensburg) Karl-Friedrich Becker (Munich), Ondrej Topolcan (Pilsen), André Gessner (Regensburg), Matthias Evert (Regensburg) and Dalibor Valik (Brno)

acronym is dedicated to the European anthem ('Every man became a brother') as a strong commitment to the European spirit. Finally, BRoTHER clearly conveys the close relationship between the network partners, which comprise a very open and trustful way of interaction.

Within this project a network is created, which actually consists of four partners, two in Bavaria (Germany) and two in the Czech Republic. The German partners of the network are the Institute of Pathology of the University Regensburg, which function as the co-ordinator of BRoTHER and the Institute of Pathology of the Technical University Munich. The partners of the Czech Republic are the Department of Immunochemistry of the Faculty Hospital Pilsen and the Masaryk Memorial Cancer Institute from the Faculty of Medicine of the Masaryk University in Brno (Fig. 3). As a brand for this project, a logo was designed by a professional communication design agency (<http://www.gruene-kd.de/>). The philosophy behind the brand development was to symbolise both the close connectivity of the partners and the openness of the network for potential new partners in the region (Fig. 4).

The vision of BRoTHER is to facilitate the interaction and co-operation of the biobanks with help of digitalisation. To reach this goal, BRoTHER is aimed to create an interactive, interregional biobank network in the centre of Europe, to harmonise biobank infrastructures, and activities related to the effective international collaboration and experience exchange, workflows and the integration of study programme development. The main topic in that aim is to consider the regional specificities resulting from the fact that the network acts in different healthcare systems and from the fact, that this regional network is located in a former region of a nearly closed border. The latter was a relevant issue for the funding which aims to the regional development of the ancient border region

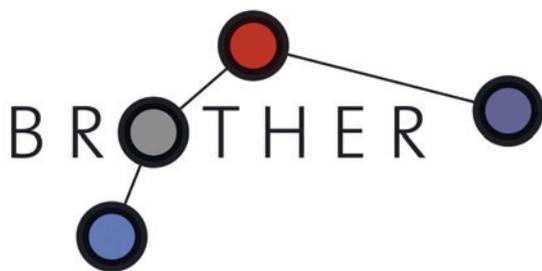


Fig. 4 The BRoTHER-logo: BRoTHER is an acronym for Biobank Research on Telemedical Approaches for Human Biobanks in a European Region. The round dots represent the biobank locations in the colour of the corporate identity (blue for Munich, grey for Regensburg, red for Pilsen and dark blue for Brno). The orientation of the dots represents the geographic situation of the four partner sites. The lines between the dots symbolise the close connectivity of the network. However, the connectivity by the line drawings is not closed which symbolises the openness for potential new partners (The logo was designed by Grüne Kommunikationsdesign, www.gruene-kd.de)

with the goal to give further incentives for a regional co-operation especially at the level of academic co-operation and exchange. In this context, BRoTHER will support the initialisation of clinical trials with biobank specimens between Bavaria and the Czech Republic. With the location in the centre of Europe the network will represent a unique example for effective inter-regional co-operation in Europe and thus could act in the future as an innovative nucleus for interconnected biobanking.

With view to digitalisation of the interaction of biobanks, we will create a prototype of a digital pathology framework in which secondary consultations regarding biobank-specimens could be conducted remotely for accurate tissue diagnosis and the potential use in a research project. Therefore, we believe that employing the mature enough Whole Slide Imaging (WSI) and Virtual Microscopy (VM) technologies in a regional network of tissue biobanks will not only provide access to such expertise but will also create new research projects within that network.

Furthermore, by comparing the produced histological slides of the stored tissue samples between the connected biobanks, an interactive discussion regarding tissue storage and pre-analytics will be promoted. Therefore, our framework will include the possibility of interactive standard operation procedure (SOP) – development regarding tissue sampling, pre-analytics and tissue storage techniques. Thus, the network will promote future collaboration projects due to harmonised SOP's.

Finally, a so-called minimal-information set regarding the histopathological information, which should be part of a biobank specimen evaluation prior to potential inclusion in a research project will be established. To train the handling of the digital pathology framework and the application of the SOP's within the infrastructure of the connected biobanks, a training programme will be established for biobank staff. After the three years of developing and evaluation this workshop will be open for all interested members of human biobanks. In addition, through public events the consortium will inform the public in the participating regions regarding the need and the function of biobanking for healthcare, especially with view to the need for collaborative work of biobanks. Consequently, BRoTHER will integrate both, the interregional co-operation on the scientific but also on the public level.

The architecture and organisation of BRoTHER

The architecture of the project and the biobank network is based on four main topics. The backbone of the project will be the digitalisation and interconnection of WSI and an interactive digital pathology framework for interactive secondary consultations. In this context, the project partner will

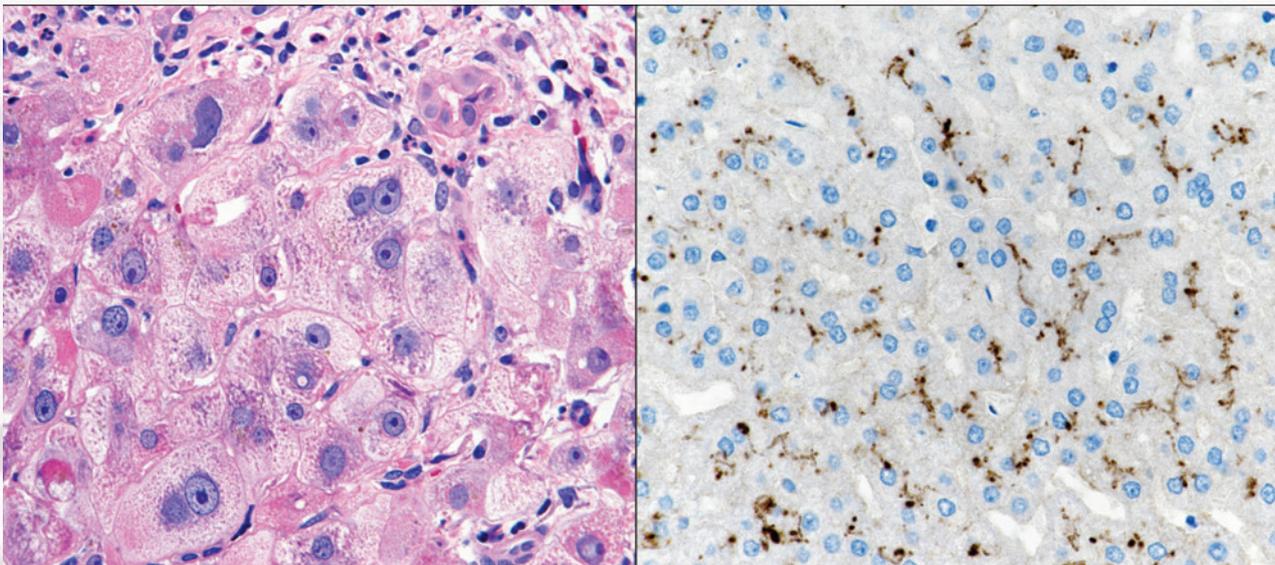


Fig. 5 A special issue of the BRoTHER consortium represent a Whole Slide Imaging tool for interactive second opinion process for histopathological evaluation of tissue biobank specimens.

also make efforts in the complex field of extraction and digitalisation of a data from pathological reports. Furthermore, the comparison of the pre-analytic procedures at the partner biobanks as well as its digitalisation will be crucial pre-requisites for the future initialisation of common research projects. Another important topic represents the dissemination of biobank knowhow and public relations, which will bring the biobank idea nearer to students of science and medicine but also to a broader public in the region. Finally, special attention will be given to the co-ordination and the management of the network, which will be crucial for the successful interconnectivity work. In this field, the organisation of workshops, symposia, a summer school and a student exchange between the participating biobanks will be organised.

Each project partner is responsible for one of the main topics and will share the knowledge with the partners. In addition, each partner will participate within the other main topics, so that the specific conditions of each partner sites will be taken into account within the different topics. This will be an important prerequisite for potential harmonisation of the workflows at each partner site.

To really and effectively interconnect the partners, workshops, symposia, summer schools and student exchange programmes will stimulate the harmonisation process. With public events the project partners will not only sensitise the public in Bavaria and the Czech Republic for the need of biobanking to optimise personalised medicine, but also for the need of inter-regional research activities.

Digital pathology – a backbone for biobank interconnection

In the BRoTHER, network digital pathology will give the virtual filament which builds the connection of the

partners. The aim is to interconnect the partner biobanks via a digital pathology framework based on WSI. This will facilitate both the interactive and easy to handle exchange of imaging data and a tool for secondary consultations of histopathological features. These features will facilitate the establishment of common projects because the availability of appropriate biobank specimens could already be checked in the planning phase of a project. Furthermore, if a project protocol requires secondary consultations of histopathological data, this could be easily performed interactively within the project if it is performed with the project partners.

The first step to reach this goal is to create a prototype of a digital pathology framework. For this purpose, we use modern web-based technologies for WSI and virtual microscopy (Fig. 5). These parameters are crucial prerequisites to develop a tool for sharing histological image data and interactive image evaluation. As a base for this development the framework of 'Pate' will be used.^{2,3} Originally developed as a user-friendly e-learning tool to teach histopathology, this tool was awarded the highest German academic teaching award, the 'Ars legendi Award' in 2015, by the German Medical Faculty Day.⁴ After transforming this platform from German into English for its international use, we will modify the Pate tool to create a prototype of a digital pathology framework to use it for interactive reference pathological analyses. In this context, it is crucial to optimise the tool for both desktop and small screens. Via several feedback loops during the development of the framework we will optimise it to realise a smart and user friendly online consultation system. Regarding the development of such a system the consortium partners profit from the experience in the application of modern telemedical approaches in the academic pathological field by one of the project

partners.⁵ The important value and accuracy of telemedical approaches for pathological diagnostics was demonstrated not only within the workflow of histopathological diagnostics but also with view to 3D microscopy.^{6,7}

For the application of such a tool in clinical or research practice respectively, it is important to guarantee safe and unique access to this digital system during image sharing. For this purpose, a special software will be used.

An important issue of the BRoTHER consortium is to disseminate the knowledge and relevance of modern information techniques for both disciplines namely biobanking and modern pathology. Therefore, the project partners are organising workshops and symposia. The aim of these events is to make graduate and post graduate students, but also researchers and technical staff familiar with the art of modern web technologies and with the potency of their application in biobanking and digital pathology. The most important feature in this regard represents the graduate and doctoral students exchange between the laboratories of the partner sites. Students from all the partner sites have the opportunity to work in the project via an exchange programme. The project partners also integrate the public since the need for interactive and interregional biobank research will be presented in public lectures. With that also the public will learn about the importance of biobanking and the participation to optimise personalised medicine. The organisation of these events will be illustrated below.

Pathological reports – a treasure and challenge for data extraction and use in biobanking

Pathological reports, especially the histopathological reports, represent valuable sources for relevant information regarding the specific type of a lesion, the exact dimension and the extent of a lesion with view to the potential affection of the surrounding tissue. Furthermore, general tissue reactions which are accompanied by specific lesions such as necrosis, inflammation, fibrosis, regeneration and wound healing are classified in the histopathological report. From special value are the histopathological reports of malignant tumours since they include important information regarding staging and grading but also the expression of specific prognostic markers, as well as the expression of molecules which are targets for innovative therapeutic strategies in the cadre of personalised medicine. The goal of these new strategies in oncology is to treat malignant tumours more specific, more effective and with less side effects.⁸ A special challenge represents malignant tumours in children and young adults which could achieve long-term remission using mainly conventional treatment regimes in approximately 80%. However, a relevant number of children and

adolescents die every year caused by malignant tumours, for which reason cancer remains a major cause of morbidity and mortality in this population.⁹ Even if the reasons for that situation are multifactorial, specific characteristics of tumours in this age group represent one of these reasons. In this context, the histopathological reports include information regarding cellular characteristics and relevant tissue parameters such as vascularisation of tumours, the proliferation of the tumour cells, the immunological reaction of the surrounding tissue as well as the aggressiveness and the invasiveness of the tumour. Especially from the scientific point of view the digital extraction of relevant information out of the histopathological reports would be of special interest for both a better understanding of the tumour biology and the definition of new targets for potential new treatment strategies. The vision is the extraction of relevant information and the digital integration within a biobank data management system. One way to reach this goal would be the use of structured formalised histopathological reports instead of unstructured continuous text which is mainly reality for pathological reports.

From the pathological point of view, the continuous text more likely gives the possibility to express subtle but relevant information regarding different levels of informative parameters and their relationship with view to the pathological relevance of the morphological findings. However, each pathological report finishes by a distinct epicrisis, which clearly define the anatomic-pathological lesion, its grading and the relevant information which is important for recent therapeutic strategies. In fact, the epicrisis represents the critical conclusion of the histopathological findings. Nevertheless, the information which is given in the histopathological description within the continuous text is of special importance, first because it gave the rational base for the epicrisis and second because it contains a huge amount of information which could be relevant for scientific use. Especially within the further development of personalised medicine the histopathological findings could help to describe specific tumour characteristics as well we potential therapeutic and prognostic factors respectively.

Taking these issues into account it is of special interest not only to extract information regarding the tumour entity, its stage and grade out of the pathological record but also information from the histopathological description. Data extraction out of a formalised text or out of a structured text given in a table or which represent more thesaurus as a text might be easy to extract by digitalisation. However, the extraction of information out of a continuous text represent a huge challenge. As a first approach to this complex field within BRoTHER, we compare the structure of pathology reports especially from tumour patients at all partner sites, followed by an analysis of its level of



Fig. 6 a proper documentation of the pre-analytical workflow is given by a code-driven specimen-tracking system, which enables the connection of the specimen with further data such as pre-analytical parameters, clinical data as well as laboratory data and imaging data

formalisation. This topic of BRoTHER is also open for the student exchange programme.

Graduate and post graduate students from one partner site visit the pathological institute of the other site and will have the opportunity to analyse the pathological report preparation, the content of the reports as well as their structure and their level of formalisation. As a result of these visits, formalised structure organograms of the pathological reports of each site will be accessible, which will be compared within a workshop. Furthermore, within the same visit students will evaluate the needs for pathological report data at the biobanks of each site as a base to create a so-called 'minimal information set', which will also be performed during a workshop with the students and the researches of the partner sites. The definition of this minimal information set could then be implemented within the biobank concept at each partner site. Finally, concepts will be created to set up a system for collecting data out of pathological reports to be acceptable for all partners and in accordance with the system proposed by BBMRI-ERIC.¹⁰

Comparative pre-analytical assessment and digitalisation

An important prerequisite for effective interconnection and potential co-operation of several biobanks represents the harmonisation of the pre-analytical assessment, its monitoring and its documentation (Fig. 6). Furthermore, the documentation should be visible for the project partners, for example as defined levels of quality. In this context, the development of a

detailed concept for the biobank quality management for both body fluids referring to 'liquid biobanking' and body tissues referring to 'tissue biobanking' are addressed in great European consortial projects.¹¹ These initiatives also include great efforts for the standardisation of generic pre-analytical procedures for *in vitro* diagnostics in personalised medicine.¹² The definition of consistent quality parameters to reach homogenous biological quality due to harmonisation of the pre-analytical conditions in biobanking is recently a matter of a broad debate.¹³ With this regard, several multicentre trials regarding measurement of tissue quality as a function of the numerous processing alternatives especially as a function of different tissue fixation were done.¹⁴

In the BRoTHER consortium we will evaluate the national and international recommendations for pre-analytical pathways and storing conditions to find ways for their proper implementation in the workflows of the partner sites. We started with the analyses and the comparison of the pre-analytical pathways of biobanks with the project partners and analysed the ratio behind these. Since biobank workflows within biobanks dealing with patient biomaterials have to be applicable at the interface of the clinical workflow and that of the local biobank, local conditions and pre-requisites for specimen samples have to be taken into account for the harmonisation and the implementation of national and international standards respectively. From the pathological point of view, the workflow of tissue sampling, processing and storage is of special interest.



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These processes may be influenced for example by the fact that the operative theatre is not in the same building as the biobank with consequences of the time for cold ischaemia and for the mode of transportation. Another relevant point represents the protocols for tissue processing, paraffin embedding and the staining protocol and procedure. Therefore, within the BRoTHER consortium the workflow and protocols for the histological slide production at each site will be analysed and compared with that of the partners. In addition, we compare the histological staining results as a function of pathological interpretation and potential influence of the scanning results during whole slide imaging for the digital second opinion workflow. We feel that these processes are important pre-requisites for the effective harmonisation of standard operation procedures with the project partners. Furthermore, the partners actively take part in the optimisation of workflows and standard operation procedures during the harmonisation processes. Finally, for an effective co-operative work and a real initialisation of common projects an appropriate service unite is necessary which will be implemented in the BRoTHER partner sites.¹⁵

To get BRoTHER known - dissemination of biobank knowhow and public relations

A critical issue in modern biobanking represents their sustainability. Beside appropriate financing of a biobank infrastructure the acceptance in the public and the exchange of knowhow are crucial parameters to

guarantee both, the long-term biomaterial donation by the patients or the population respectively and the continuous work with state of the art methods. Furthermore, dissemination is also an important feature to be attractive for and to get access to the potential participation in new experimental studies or trials initialised by third parties. To disseminate and promote the ideas and the activities of BRoTHER posters, presentations at relevant conferences and events, brokerage events, development of information materials in the languages of the involved partners, namely in German, English and Czech will be used in co-operation with all partners. In this context, the publications with the Pan European Network represent a further strategy of dissemination, namely to make BRoTHER known and attractive to the readership from the European Parliament, the European Commission but also for European and national research grant agencies.^{16,17} Altogether, this chapter of our dissemination activities address the scientific community.¹⁸ However, for the latter the most important parameter to attract a biobank for potential new partners is the scientific activity of a biobank especially with view to high quality and innovative trials with biobank specimens.^{19,20} Therefore, it is crucial for all biobanks and also for our BRoTHER consortium to publish research data in peer reviewed journals as original research papers which are visible in relevant data bases such as EMBASE or Medline.

The dissemination of biobank knowhow to a broader public and the work on public relations is important

for two reasons: the first is to stay attractive for potential biomaterial donors and gain or keep the acceptance of the biobank within the public. Finally, dissemination of biobank knowhow will also be an instrument to enlighten to the public the need of biobanking, its role for personalised medicine and its role in modern biomedical research.

To address this issue, press releases and short information as well as articles in magazines, journals, and other printed materials has already and will be published regularly both in Bavaria and the Czech Republic. In addition to that, national press releases will provide information on the most important initiatives promoted and organised by the project at national level. Furthermore, co-operation with relevant associations, infrastructures and other relevant partners will be initiated to disseminate the information on the project and to open the space for the future collaboration. In this context, the project BRoTHER and the need for biobanks and biobank research was presented to the public by the official opening ceremony of the opening of the biobank at the Faculty Hospital Pilsen in the beginning of 2017. Furthermore, BRoTHER was already presented by different workshops at the Immunoanalytic Days Pilsen 2017 and 2018 to a broader academic public.

Self-organisation and project management of BRoTHER – working together and learning from each other

An important aim within the BRoTHER consortium is learning from each other by working together. With view of the different levels of interconnection and co-operation, as well as with view to harmonisation of processes the project partners compare their workflows, analyse its ratio behind it and evaluate if these are appropriate with national and international standards in biobanking. Therefore, self-organisation is another crucial part within the project, which co-ordinate the organisation of the workshops and symposia, and the interactive work among the partners.

Furthermore, the organisation will co-ordinate the writing and the allocation of the annual progress reports as well as the final report at the end of the project. This is done by the co-ordinator of the BRoTHER project which is the institute of pathology of the University Regensburg. A crucial element of this interconnected work represents a student exchange programme of graduate and post graduate students. They will be integrated in the different aspects of harmonisation and digitalisation. They will rotate from one partner to another and will be actively integrated in the project work and in the infrastructure of the different biobanks at the partner sites. With that the students will become familiar with work flow, the analyses methods and the standard operation procedures at the different partners of BRoTHER. Thus, they will learn more about the

project partners of the other country as well as how the recent developments in whole slide imaging and biobanking give support to the project.

The main elements of the self-organisation and management is the organisation of workshops, symposia, summer schools and public events. These several types of events should make the interconnective work of the BRoTHER consortium known. Furthermore, these events act as a forum for the project partners to get informed and to discuss the state of the harmonisation process on several levels. The different event types followed a kind of hierarchy regarding the aims and the size.

The workshops represent the smallest event type. They are organised twice a year, one with a Bavarian partner and one with a partner in the Czech Republic. The workshop will be open for the students and scientists working in the different aspects of the project. Furthermore, they will be open for students and scientists of the organising site, if they work in the same field and are interested in interaction. One important topic of the workshops is practical work on different aspects of biobanking. The subjects of the workshops are Biobanking Data Management; Techniques on Whole Slide Imaging; The Effect of Pre-analytic for Biobank Specimen; and Ethical, legal and social aspects of biobanking (ELSI). Furthermore, during the run time of the project further subjects for workshops will be identified regarding the needs becoming obvious during the project work.

Symposia will be held once to twice a year in Bavaria and the Czech Republic and will bring the students and scientist of the partners together with leading researchers in the different fields of the projects. The most important topic of the symposia is the presentation of the recent research topics and research trends within the field of biobanking as well as the exchange of knowledge. The first symposium was held in the cadre of the opening ceremony of the Pilsen Biobank in in 2017. The symposia will be open for interested researchers not only from the sites of the project partners but also for all interested researches in the field of biobanking.

During the funding period two summer schools will be organised in 2018 and 2019 with the aim to bring the students of the different work packages together to present and discuss their activities and results with each other and with leading researchers in the field. The idea is that the summer schools will held at each partner site so that the opportunity is given to learn more about the partner institutions and the cultural aspects of the partner cities.

Not only during the funding period but also after that time several public events will be organised to present the consortium and its activities to the public and to sensitise the public for the need of biobanks,

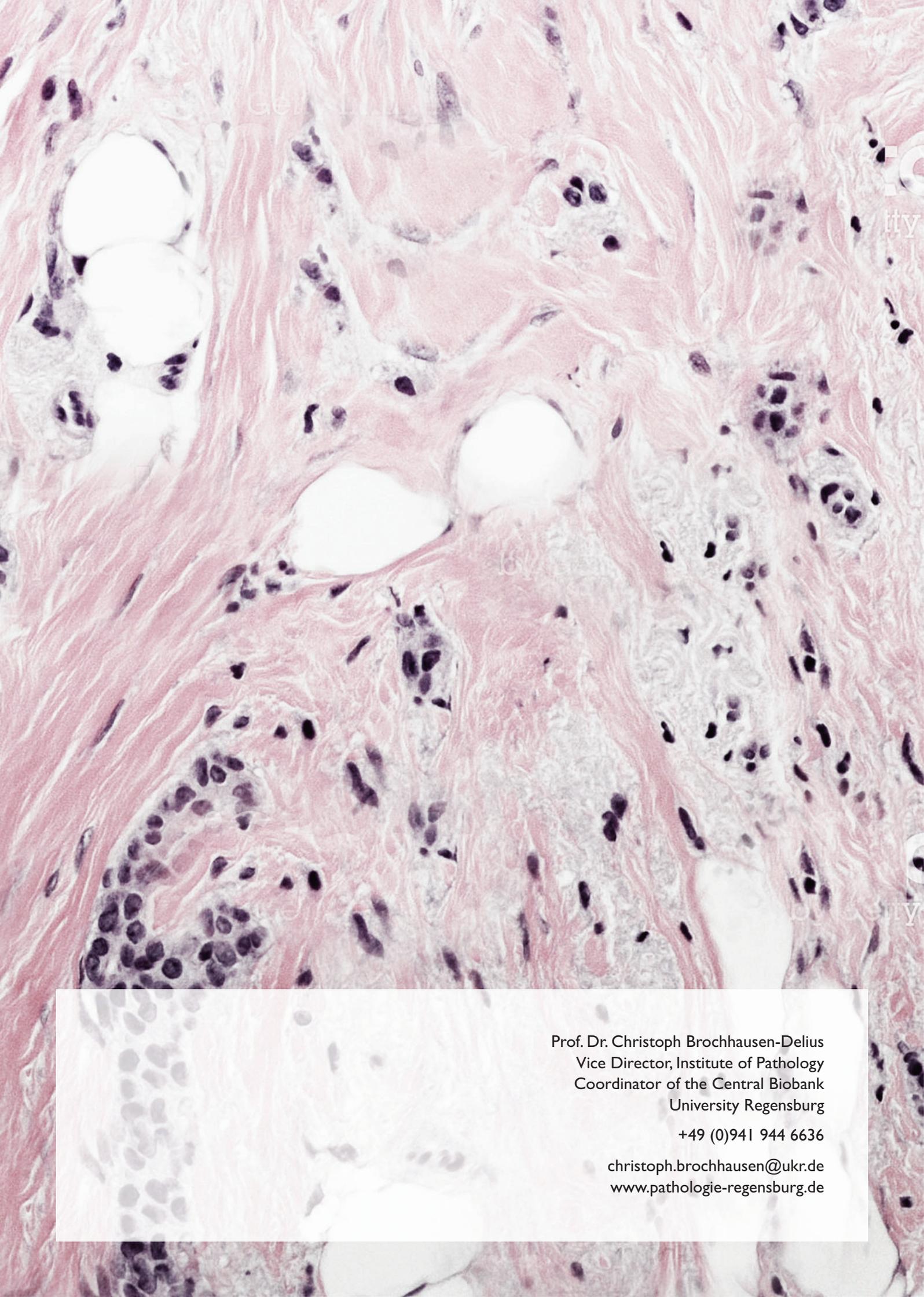
interregional biobank research and the function of biobanking in modern medicine.

Future vision

In conclusion, BRoTHER represent an interactive, interregional biobank network in the centre of Europe, to harmonise biobank infrastructures and activities related to the effective international collaboration and experience exchange, workflows and the integration of study programs development. The latter will be focused on graduate students in medicine since there is a need to bring the relevant subject of biobanking also in the curriculum of the human medicine. Taking all these aspects together the performance of clinical trials with biobank specimens should be facilitated between Bavaria and the Czech Republic due to the BRoTHER project. With the location in the centre of Europe the network will represent an example for effective inter-regional co-operation in Europe and thus could act in the future as an innovative nucleus for interconnected biobanking, which will be integrated in further international networks and initiatives, which are working in the dynamic field of biobanking.

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