

### 4.3 Progress report of subproject 3

**Project title:** Integrated network of the reference panel for lymph node pathology

**Project leader:** PD Dr. Michael Hummel  
 Charité - Universitätskliniken Berlin  
 Campus Benjamin Franklin  
 Institut für Pathologie  
 Hindenburgdamm 30  
 D-12200 Berlin  
 Phone: +49 (0) 30 8445 2614  
 Fax +49 (0) 30 8445 4473  
 E-mail: Michael.Hummel@medizin.fu-berlin.de

#### 4.3.1 Summary

The aim of subproject 3 is to improve and accelerate the communication between the six pathology reference centres and the clinical study centres. For this purpose, a new computer-based infrastructure was constructed to allow for the fast and reliable exchange of patients' information. This exchange of information is based on a common data bank structure employing local databases at the reference centres for lymph node pathology, the clinical study centres, and a central pathology database at the Institute of Medical Statistics and Epidemiology (IMISE) at the University of Leipzig. On the basis on this structure, we can immediately identify patients enrolled in clinical trials and have access to the reference-pathological diagnosis before initiation of the patients' treatment.

#### 4.3.2 Results and ongoing activities

The identification of patients enrolled in clinical trials in the reference centres for lymph node pathology is a basic step. In most cases, which are sent to the reference centres, it is not known whether the lymphoma patient should be enrolled in a clinical trial. The reference-pathological diagnosis is therefore not transmitted immediately to the study centre of the corresponding clinical trial. Due to the slowness of paper-based information transmission, the reference-pathological diagnosis is often only available after initiation of treatment. Since the reference-pathological diagnosis differs from the initial diagnosis by up to 40% (depending on the lymphoma disease entity), the availability of the reference-pathological diagnosis prior to the initiation of the treatment is highly desirable.

As a result of the work of the subproject 3, the immediate identification of patients enrolled in clinical trials is now an established concept. The clinical study centres send the names of potential patients to be enrolled in the respective clinical trials to the central pathology server at the IMISE in Leipzig on a daily basis. From there, the data are sent to the various reference

centres for lymph node pathology where they are compared to the local database. The information from patients who matched on the criteria *Christian name, family name, gender and age* are immediately delivered to the pathologists in the reference centres where the patient was originally identified. Based on this information, the diagnostic process is adapted for patients enrolled in clinical trials.

In order to allow the automatic transmission of diagnostic results to the clinical study centres, the databases of all local pathology IT systems need considerable modification. This requires the development of a modified database structure in close cooperation with the designers of the commercial pathology IT systems (DC PATHOS available from DC SYSTEME [running in Berlin, Frankfurt and Ulm] and PAS available from PASCHMANN [running in Kiel, Lübeck and Würzburg]) currently in use. In parallel to these planned modifications to all local pathology IT systems, the classification of malignant lymphomas also has to be adapted to fulfil all criteria required for pathologists and clinicians. This work was recently undertaken by a panel of reference pathologists, based on the new WHO classification of malignant lymphomas, taking the most recent developments into consideration. This adapted lymphoma classification is now available, and is currently embedded in all the local pathology IT systems, as well as in the local and central data bases of subproject 3.

A further major task undertaken during this funding period was the evaluation of our data protection concept. We initially contacted the data-protection authority responsible for Berlin ("Datenschutzbeauftragter" Berlin, the coordination of subproject 3 is located in Berlin), and they duly accepted our application. Some concerns were however raised by the data-protection authority in North Rhine-Westphalia (NRW) due to the fact that the entire Competence Network Malignant Lymphomas is coordinated from Cologne. Since there is no data protection concept that covers all subprojects of the network, the question whether it would be possible to incorporate subproject 3 in a network-wide data protection concept arose. Discussions with the authorities in NRW disclosed that a network-wide data protection concept could be developed in the course of the following few months, whereas a data protection concept exclusively for subproject 3 would be required earlier. An agreement was therefore reached that the data-protection authority in Berlin should complete the evaluation process for subproject 3. At the time of writing this report, this was nearly complete.

Based on our first experiences gathered by our communication infrastructure, several improvements have been introduced. A major challenge in this respect was the stabilisation of the data transfer. It came to our attention that in the case of large data sets in particular, there were often interruptions to the connection. To overcome this problem several modifications were introduced, including intensive control of the complete transfer, and the re-establishment of interrupted connections. Furthermore, the Internet-based interface, which was designed to search for study patients' diagnostic information and to complete (as long as the automatic re-

transmission of diagnostic information has not been established on a routine basis) diagnostic information, was adapted in several steps to the demands of the pathologists.

In March 2003, the second funding period of subproject 3 started. Within the next two years we plan to extend our infrastructure to the online and offline exchange of histological images. The online image exchange will be based on conventional video technology directly connecting two or more pathologists to enable the discussion of difficult lymphoma cases. This will speed-up the reference-pathological diagnostic procedure, especially in difficult cases. The offline exchange of images is intended to support panel meetings of reference pathologists (histology of 20% of patients in each clinical trial is re-evaluated at common sessions) at multi-headed microscopes. This is very time consuming, but at present there is no alternative based on conventional histological glass slides. The intention therefore is to digitise the histological sections of these cases (20%) and to make them available for evaluation via Internet.

#### **4.3.3 Cooperation within the network**

Broad ranging cooperation is being established between subproject 3 and the subproject responsible for the acquisition of fresh frozen material from study patients, subproject 13. Since frozen material will be stored in the respective reference centres for lymph node pathology, and the corresponding patient information will be filed in the central pathology database, close cooperation between both subprojects is mandatory. Moreover, close cooperation has also been agreed with respect to all data protection aspects.

#### **4.3.4 Other cooperation**

The introduction of advanced technologies for the acquisition and processing of very large images, which need to be generated in the course of the digitalisation of entire tissue sections, requires close interaction with companies active in this field. The initial plan was to digitise whole tissue sections by means of motorised microscopes, however more and more techniques are becoming available to simply scan in glass slides, in one single step. Subproject 3 will therefore intensify its association with the respective companies active in this field, in order to exploit the new technologies available.

#### **4.3.5 Publications**

- Speer R., Hummel M., Heller B.: Vernetzung der Referenzpathologien für Lymphknotendiagnostik und Aufbau einer virtuellen Materialdatenbank. Informatik, Biometrie und Epidemiologie in Medizin und Biologie. 2001; Band 32: 300-301

- Hatje H., Speer R., Heller B., Noack F., Stein H., Hogrefe D., Feller A.C., Hummel M.: Lymphknotenreferenzzentren: Aktuelle Online Studienpatienten- und Materialdatenbank. In: Telemedizinführer Deutschland, Ausgabe 2003, S. 100-103

#### **4.3.6 Further objectives for the current funding period**

In the forthcoming period effort will be focused on establishing the online and offline discussion of lymphomas cases. Whereas the online discussion will be based on commercially available systems, the offline discussion is a brand new field, which will require a great deal of attention. However, the most recent technical developments appear to be the most suitable for our purposes, enabling the acquisition of whole tissue sections, including their storage in high capacity file servers. Although the images obtained from whole tissue sections are extremely large (150 MB after compression; 2 GB without compression), high quality rapid transfer of the images will be possible via internet as only the requested proportion of the slide needs to be transmitted, and not the whole image as one file. We are convinced that this technology (also referred as to "virtual" or "digital" microscope) will significantly improve and speed the work up within each reference centre of lymph node pathology as well as with the clinical study centres.