EC COST B21: Physiological Modelling of MR Image Formation

WG3: Experimental verification and trials.

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WG3 is dedicated to experimental verifications and trials. As well, it concerns several different steps of the COST B21 programme:

1. Technology transfer, i.e. the transfer of emerging MR technologies mainly developed in WG1 to other groups in order to validate the methods. In this first step, the biological meaning of the results is not deeply analysed and it is too early to start large multicenter clinical trials. Presently this step can, for instance, concern phase related information (tissue oxygenation, relative blood volume, perfusion vectors…): this technology transfer will mainly be managed into WG1.

2. Preclinical trials: This second step concerns the implementation of the new methods on experimental MRI-MRS devices (usually at higher fields) in order to:

   - Optimize the acquisition parameters
   - Correlate the MR extracted data with biological data on animal models (more standardised that human pathologies)
   - Determine the biochemical rationale of future clinical trials

   This second step is clearly a task of WG3 and implies the exchange of animal models and biological expertises.

3. Clinical trials: the clinical validation of a new method can only be realized on rather large patient populations, in multicenter trials and using high standardized protocols (image acquisition, image processing, additional bio clinical data, data analysis, quality assessment…). Among

the methods initiated or developed in the COST B21 program, only few can presently generate a multicenter trial.

For the clinical and preclinical trials, the expertises of the COST B21 participating groups orientate the evaluation methods on only two pathology families:

- Brain tumours (BT)[1]
- Liver precancerous disease (LPD)[2]

Then the proposed tasks for the next year (2005) can be summarized as presented in the following table.

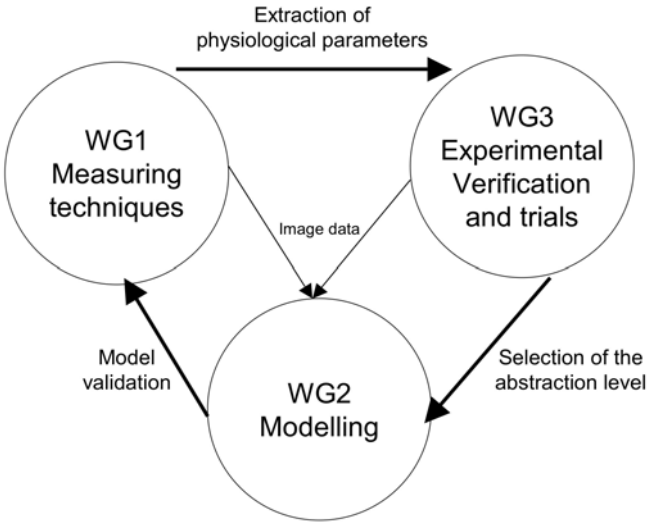
NMR METHODS	TECHNOLOGY TRANSFER	PRECLINICAL TRIALS (WG3)	CLINICAL MULTICENTER TRIALS (WG3)
SWI, FLOOD, OEF…	BT (WG1)		
2D-TA	BT-LPD (WG2)	LPD	BT, LPD
3D-TA	BT-LPD (WG2)		BT (?), LPD (?)
DER	LPD (WG3)	LPD	BT, LPD (*)
31P CSI	LPD (WG3)	LPD	LPD (*)

(?) Depending on a preliminary step of technology transfer (probably in 2006)
(*) Depending on the number of clinical groups able to participate
SWI: Susceptibility Weighted Imaging
FLOOD: Flow and Oxygenation Dependant Contrast
OEF: Oxygen Extraction Fraction
TA: Texture Analysis
DER: Dynamic Enhanced Relaxometry
CSI: Chemical Shift Imaging

The specific role of WG3 and the complementarity between WG1, WG2 and WG3 into COST B21 programme is illustrated by the following scheme.

[1] COST B21 groups involved in brain oncology (NMR units working on 3T systems in 2005 are underlined): JENA, HEIDELBERG, RENNES, SURREY, PRAGUE, MARTIN, VIENNA, BERGEN, BRATISLAVA, TRONDHEIM

[2] COST B21 groups involved in hepatology (NMR units working on 3T systems in 2005 are underlined): RENNES, PRAGUE, SURREY, MARTIN, VIENNA, DUNDEE



This diagram demonstrates that verification and trials are not only the "front end" of COST B21 but that an important feedback exists from verification to modelling and from modelling to method design.

The important problem of the "gold standard" for clinical results validation has been discussed. In several clinical problems, such as the grading of gliomas or the prognosis of precancerous liver diseases, a "gold standard" does no exist or is not satisfying as many discrepancies have been described between pathology and the disease evolution. Then, in our opinion, functional MR imaging as developed in COST B21 has exactly the same challenge than genomics and proteomics, also questioning the presently used diseases classification. It means that functional imaging, as a part of metabonomics, genomics and proteomics will have to associate and compare their new data.

The following goals and milestones have been decided for the period end-2004 to early 2006:

BRAIN TUMOURS

Before November 2004, the Rennes group will send to all potential participants listed above the draft of a protocol concerning:

- Dynamic Enhanced Relaxometry (DER)
- 2D Texture Analysis (2D-TA)

The protocol will concern high and low grades glioma and can be performed in routine clinical unit without significant modification of the acquisition protocol. Five phantoms filled with substances of known relaxation times will be provided by Rennes to each participating group for

quantitative DER. A preliminary MRI quality assessment protocol will be also proposed.

LIVER PRECANCEROUS DISEASES

Preclinical studies

Draft protocols will be proposed by Rennes for 2D-TA and DER and by Prague for 31P CSI as soon as possible.

An exchange of experimental animal models (cirrhosis, steatosis, iron overload, tumour, liver regeneration) will be organised in order to provide each potentially interested group with well evaluated and standardised models. It should be interesting to test SWI on some of these models.

A questionnaire will be sent to all groups performing experimental studies on mice and rats before the Brussels meeting (January 2005).

Clinical studies

A first imaging protocol for 2D-TA will be sent in October 2004 to Prague and Vienna in order to realise preliminary tests on 10 patients (cirrhotic liver) in each group. Images acquired in each centres will be tested by the others also.

These preliminary results will be discussed during the Brussels meeting in January before extending a standardised imaging protocol to all participants listed above.

CONSTITUTION OF A BT AND LPD DATABASES

First, a CD-ROM containing 2D and 3D BT and LPD acquisitions will be burnt and sent to the software development and image processing groups (Lodz, Guildford, Martin, Rennes…) for new evaluation of post-processing TA methods, segmentation and modelling.

Then, these databases, which will grow and evolve with time, should be accessible by the web site of COST B21.