WP 2

Clinical research infrastructure

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WP 2.1

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Concepts and terms for dose volume parameters and for outcome assessment in hadron therapy integrating applied biology, medical physics and clinical medicine in ULICE

WP 2.1

Deliverable JRA 2.1 **M18**: Harmonisation of concepts and terms for volume and dose-volume parameters in photon, proton and carbon-ion therapy

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MUW, MedAustron

D.JRA 2.1 – Harmonisation of concepts and terms for volume ... Dissemination level PU

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CAPACITIES

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Integrating Activities /e-Infrastructures/ Preparatory phase
Start date of project: 1st September 2009 Duration: 48 months

D.JRA 2.1 – Harmonisation of concepts and terms for volume and dose-volume parameters in photon, proton and carbon-ion therapy
Delivery date: M18 – 2011/02/28

WP n° and title: WP2 – Concepts and terms for dose volume parameters and for outcome assessment in hadron-therapy integrating applied biology, medical physics and clinical medicine in ULICE
WP leader: Ramona Mayer, Jacques Balosso
Reporting period: M18 – 2011/02/28

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Contribution(s):			
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Approved by TPB and CPO		signature	

Dissemination Level		
PU	Public	X
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

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https://espace.cern.ch/ULICE-INTRANET/WP2/WP21/D.JRA_2.1_HarmCon_d1.3.pdf

WP 2.1

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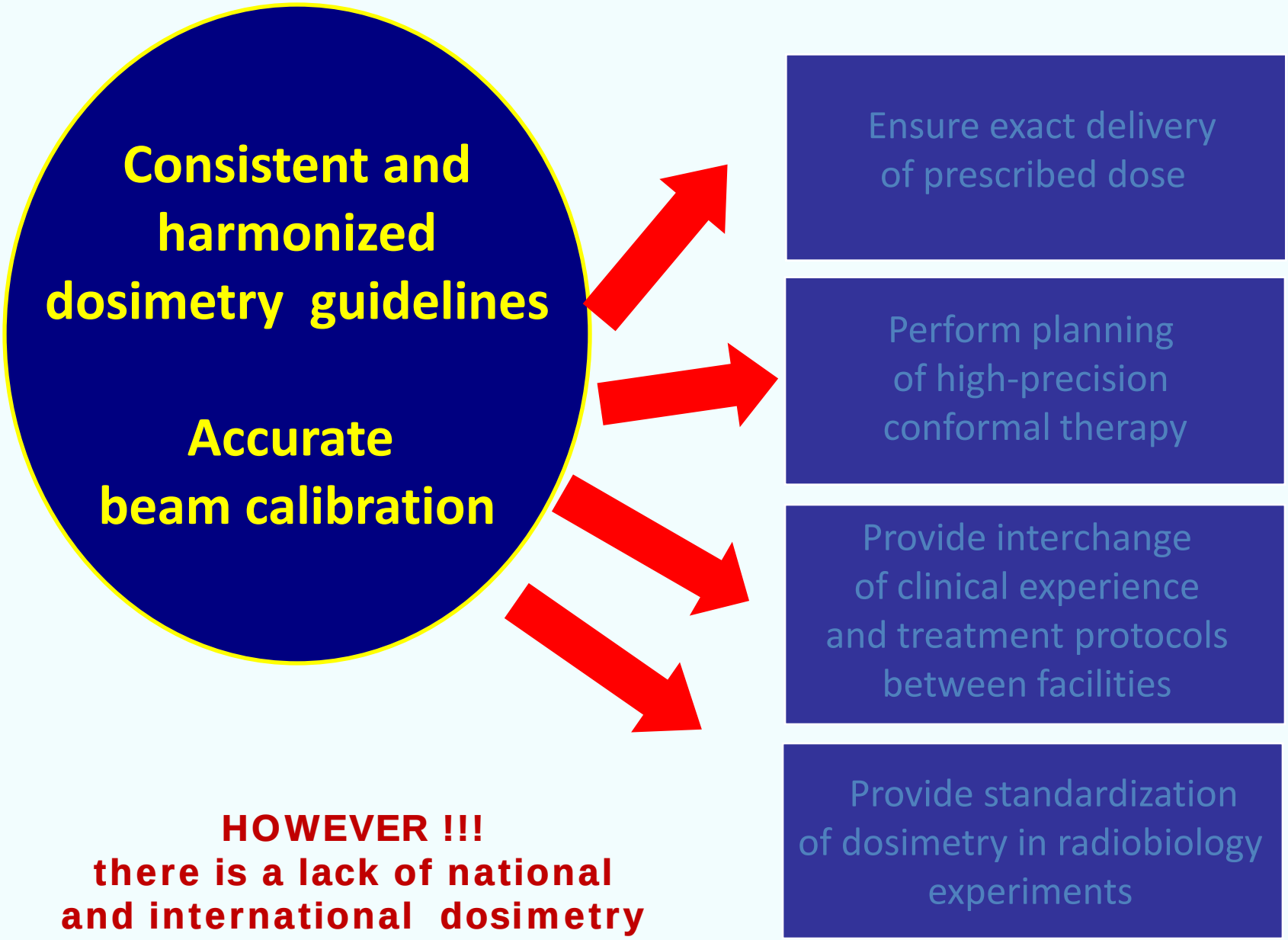
Dosimetry protocol for auditing hadron facilities participating in clinical trials

S. Vatnitskiy

MedAustron

Who, Where	Country	Particle	Max. clin. energy (MeV)	No. of treatment Rooms	Start of treatment or planned to start	Type of Beam delivery
Clatterbridge	England	p	62	1	1989	passive
Nice	France	p	65	1	1991	passive
HZB (HMI), Berlin	Germany	p	72	1	1998	passive
PSI, Villigen	Switzerland	p	72	1	1984	passive
INFN-LNS, Catania	Italy	p	60	1	2002	passive
Orsay	France	p	70, 200	2	1991	passive
Krakow	Poland	p	70	1	2010	passive
Bratislava	Slovak Rep.	p	72	1	2010	passive
St. Petersburg	Russia	p	1000	1	1975	passive
ITEP, Moscow	Russia	p	250	1.	1969	passive
Dubna	Russia	p	200	1	1999	passive
PSI, Villigen	Switzerland	p	250	1 gantry	1986	scanning
RPTC, Munich	Germany	p	250	5	2009	scanning
PSI, Villigen*	Switzerland	p	250 SCCL	3	2010	scanning
PTC Czech	Czech Rep.	p	230 CL	4	2013	passive, scanning
Trento	Italy	p	230 CL	2	2011?	scanning
CMHPTC, Ruzomberok	Slovak Rep.	p	250 SH	1	2013	passive scanning
Skandion Clinic, Uppsala	Sweden	p	250 CL	2	2013	scanning
RPTC, Koeln	Germany	p	250 SCCL	5	?	scanning
WPE, Essen*	Germany	p	230 CL	4	2010	scanning
CPO, Orsay*	France	p	230 CL	3	2010	scanning
CNAO, Pavia*	Italy	p, C-ion	430/u SH	3-4	2010?	scanning
HIT, Heidelberg	Germany	p, C-ion	430/u SH	3	2010	scanning
Med-AUSTRON, Wiener Neustadt	Austria	p, C-ion	400/u SH	3	2014	scanning
PTC, Marburg*	Germany	p, C-ion	430/u SH	4	2010	scanning
NRoCK, Kiel *	Germany	p, C-ion	430/u SH	3	2012	scanning
ARCHADE, Caen	France	p, C-ion	400/u SCCL	1	2014	scanning
ETOILE, Lyon	France	p, C-ion	400/u SH	3	2015	scanning



HOWEVER !!!
there is a lack of national and international dosimetry standards in hadron dosimetry

- Due to the lack of the standards dosimetry comparisons between the facilities were used as an independent auditing procedure to verify dose delivery

- Dosimetry intercomparison based on absorbed dose determination in reference conditions (similar to conventional RT) is valid as an independent auditing procedure only for passive beam delivery

- Scanning beam facilities are using multi-step dose per MU calibration and therefore require special dosimetry auditing procedure

End to end test

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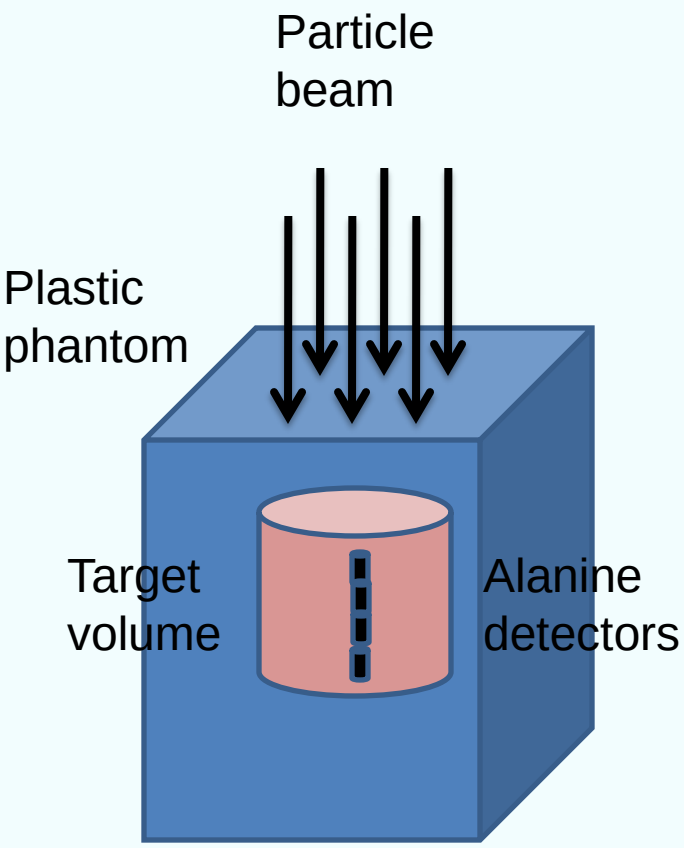
- Dosimetry protocol based on end-to-end test can be used for auditing for scanned beam dose delivery

- The purpose of end-to-end test is to confirm that the entire logistic chain of radiation treatment starting from CT scanning, treatment planning, monitor calibration and beam delivery is operable and leads to the desired results with sufficient accuracy.

End to end test

- Plastic phantom with alanine detectors
- CT-based treatment planning to deliver prescribed dose (physical dose) to the target volume within the phantom
- Positioning of the phantom and irradiation in a clinical beam



Proposed steps to establish end-to-end test dosimetry auditing procedure for scanned beam facilities (1)

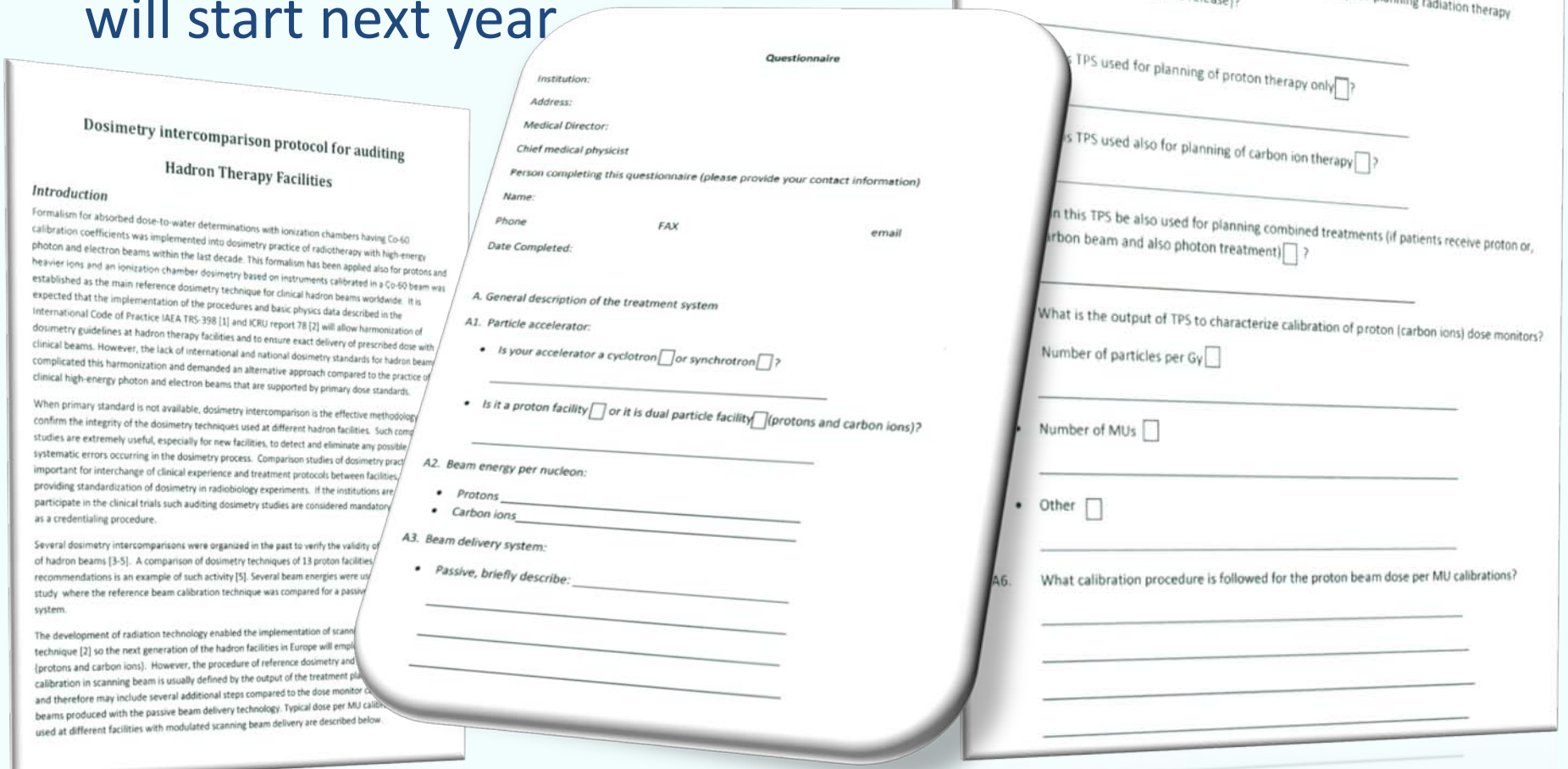
1. Develop a questionnaire and distribute it to the running European hadron therapy facilities and also to those who will start next year

2. Analyze received information on features of the beam delivery system, dose per MU calibration, and treatment planning system output

3. Get comments on the draft of the end-to-end test for dosimetry auditing.

Proposed steps to establish end-to-end test dosimetry auditing procedure for scanned beam facilities (1)

1. Develop a questionnaire and distr
   European hadron therapy facilities
   will start next year



Dosimetry intercomparison protocol for auditing

Hadron Therapy Facilities

Introduction

Questionnaire

Institution:

Address:

Medical Director:

Chief medical physicist

Person completing this questionnaire (please provide your contact information)

Name:

Phone FAX email

Date Completed:

A. General description of the treatment system

A1. Particle accelerator:

- Is your accelerator a cyclotron ☐ or synchrotron ☐?
- Is it a proton facility ☐ or it is dual particle facility ☐ (protons and carbon ions)?

A2. Beam energy per nucleon:

- Protons
- Carbon ions

A3. Beam delivery system:

- Passive, briefly describe:
- Scanning beams, briefly describe:

A4. What treatment planning system is used at the facility for planning radiation therapy (manufacturer, software release)?

TPS used for planning of proton therapy only ☐?

TPS used also for planning of carbon ion therapy ☐?

this TPS be also used for planning combined treatments (if patients receive proton or, rbon beam and also photon treatment) ☐?

What is the output of TPS to characterize calibration of proton (carbon ions) dose monitors?

Number of particles per Gy ☐

Number of MUs ☐

Other ☐

A6. What calibration procedure is followed for the proton beam dose per MU calibrations?

Proposed steps to establish end-to-end test dosimetry auditing procedure for scanned beam facilities (1)

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Proposed steps to establish end-to-end test dosimetry auditing procedure for scanned beam facilities (2)

- To finalize methodology of end-to-end test procedure for dosimetry auditing of scanned beam delivery (cooperation with National Physics Laboratory, UK)

- To organize a pilot study to test the methodology for dosimetry audit in scanned beam delivery (any new starting facility – possible CNAO)

WP 2.2

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Development of Standard Operating Procedures (SOP) for clinical trial design in hadron therapy

U. Mock, R. Mayer

EBG MedAustron

Structure analysis of existing clincal protocols in photon therapy

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Selection criteria

- Open access to study protocols
- Multicentric studies
- Investigators: RTOG, EORTC, Deutsche Krebsgesellschaft
- Radiotherapy as a main treatment option

Study analysis I

Multicenter pilot study

- Therapie von Medulloblastomen des Erwachsenenalters (NOA-07), Neuroonkologische Arbeitsgemeinschaft (NOA) in der Deutschen Krebsgesellschaft (DKG)

Phase II trial

- A Phase II Trial of stereotactic body radiation therapy (SBRT) in the treatment of patients with operable stage I/II Non-small cell lung cancer (RTOG 0618)
- A randomized phase II study comparing 2 stereotactic body radiation therapy (SBRT) schedules for medically inoperable patients with Stage I peripheral Non-small cell lung cancer (RTOG 0915 (NCCTG N0927))
- A phase II trial of image guided preoperative radiotherapy for primary soft tissue sarcomas of the extremity (RTOG 0630)

Study analysis II

Phase III trial

- Radiotherapie versus Radiotherapie plus Hormontherapie bei isoliertem PSA-Anstieg nach radikaler Prostatektomie wegen Prostatakarzinom
- Prospektive randomisierte Vergleichsstudie zur präoperativen Kurzzeit-Radiotherapie versus Langzeit-Radiochemotherapie beim uT2-3 Rektumkarzinom

Randomized Phase II / III study

- Gemcitabime followed by gemcitabine plus concomitant radiation (50.4Gy) versus control after curative pancreaticoduodenectomy for pancreatic head cancer (EORTC protocol 40013-22012)

Principal structure of study protocols

- Background and introduction
- Objective of the trial
- Patient selection criteria
- Trial design/therapeutic regimen
- Radiotherapy procedure/volume definition, dose prescription
- Clinical evaluation and follow-up / endpoints
- Forms and procedures of data collection / statistical considerations
- Patient registration and randomization procedure
- Investigator authorization procedure
- References
- Appendices (TNM classification, toxicity grading scale (CTC), informed consent statement, patient information sheet etc.)

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Different approaches …..

- External audits of documented data (questionnaires only)

or

- Random sample (10% of the original data including treatment plans etc. are checked)

or

- Simulation- and verification images should be submitted

or

- Treatment plan / target volume contours / isodose distribution etc. have to be submitted on a regular basis

Study protocol guidelines

- **ECCO-AACR-ASCO** Methods in Clinical Cancer Research Phase I / II / III studies
- **EORTC** guidelines for writing protocols for clinical trials of radiotherapy (1995)
- **EORTC** Investigator´s Handbook (2002)
- **I**nternational **C**onference on **H**armonization **(ICH),**

  GCP (Good clinical practice) Guidelines for Clinical Trial Protocol development

  ICH Topics E3/E6/E9; European medicines Agency www.emea.eu.int

  (Harmonised ICH-criteria for EU, Japan and the United States)
- **Southwest oncology group** (USA): Protocol guidelines
- **Masterprotokoll** (Deutschen Krebsgesellschaft e.V. and Deutsche Krebshilfe)

- Others……

General analysis of different study protocol guidelines

Short description of a study concept

- ECCO-AACR-ASCO
- EORTC
- GCP (Good clinical practice) Guidelines
- Southwest oncology group
- Masterprotokoll

More detailed description

- ECCO-AACR-ASCO
- Masterprotokoll

Detailed description of Phase I / II / III studies

- ECCO-AACR-ASCO

Planned SOP design

„Solved questions“

- General structure/main topics of protocols
- Study in accordance to the Declaration of Helsinki
- Study in accordance to Good Clinical Practise (Harmonised ICH-criteria)

„Open questions“

- Target volume definition
- Dose prescription
- Data review management etc.

Conclusion I

- Analysis only refers to personally available protocols/protocol guidelines
- Comparison of current analysis with actual Hadrontherapy protocols has to be performed
- Main structure of ion beam SOP should correspond to current photon based instructions

Conclusion II

- Several general aspects have to be discussed:
  - **Main protocol organisation**
    - Review committee
    - Data monitoring/quality assurance programm
  - **Radiotherapy treatment planning and performance**
    - Delineation of target volumes
    - Dose prescription
    - Dose limits to organs at risk

Deliverable JRA 2.2 **M18**

Review of the existing protocol structure in large clinical research organisations (national and international) as collected by WP 10

- Up to now different **photon** based protocols have been analysed
- Existing protocols of **ion beam therapy** will be provided by WP 10 in the near future and then analysed within the next weeks…

WP 2.3

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Design and implementation of a clinical research infrastructure in ULICE

- Deliverable JRA 2.3 **M18**

Description of tasks with a proposal for potential structures for clinical research in ULICE