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Summary Report

First Research Coordination Meeting on

Heavy Charged-Particle Interaction Data For Radiotherapy

IAEA Headquarters
Vienna, Austria

6-9 November 2007

Prepared by

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April 2008

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Abstract

A summary is given of the First Research Coordination Meeting on *Heavy Charged-Particle Interaction Data for Radiotherapy*. A programme to compile and evaluate charged-particle nuclear data for therapeutic applications was proposed. Detailed coordinated research proposals were also agreed. Technical discussions and the resulting work plan of the Coordinated Research Project are summarized, along with actions and deadlines.

April 2008

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1. Introduction

Investigations of the use of "heavy-charged particles" (as compared to electrons, photons and neutrons) for radiotherapy were initiated in the early 1970s, with the Bevalac accelerator complex at LBNL in Berkeley playing a pioneer role in the utilization of heavy ions (mostly helium, argon and neon). Because of the lower production costs of protons compared with heavy ions, the use of protons in radiotherapy has become well established, and the number of patients treated by this modality is over fifty thousand. However, there is also an increased interest worldwide in the use of heavy ions, especially carbon beams, resulting in the construction of the Japanese HIMAC clinical facility in Chiba, near Tokyo. HIMAC started the treatment of patients mainly with carbon ions in 1994, and today nearly 3000 patients have been treated in this facility. The GSI heavy ion physics research facility in Darmstadt, Germany, also initiated clinical treatments with carbon ions in 1997, and their results have encouraged the development of facilities exclusively dedicated to proton and carbon radiotherapy. Proton and heavy ion therapy offer advanced cancer treatments because of their ability to delivery highly conformal dose distributions. Further, the integral dose to the patient is lower than with conventional photon treatments. To fully utilize the increased precision and dose conformity requires the use of sophisticated computer techniques for patient dose calculation, such as Monte-Carlo procedures.

The availability of high-quality cross-section data for the simulation of heavy charged-particle interactions is far from being satisfactory. Data libraries of charged-particle interactions are needed to validate the calculations using nuclear models and for direct use in other types of calculation. There are several available Monte-Carlo particle transport codes with the capability to treat the transport of nucleons, electrons, photons and heavy ions. We expect that most of the existing codes will be modified (MCNPX, Geant4, SHIELD-HIT, FLUKA, etc.) so that they can benefit from the use of updated cross-section libraries if necessary.

A consultants' meeting (CM) was organised in Vienna in November 2006 to identify the needs for comprehensive evaluated data for nuclear interaction cross-sections, including recommendations on types of nuclear data and their accuracy[1]. One further aim was to cover all steps of proton and heavier ion therapy delivery by ensuring discussions between experts in the field of proton and ion therapy, proton and ion dosimetry, and proton and ion Monte-Carlo simulations. The following main recommendations were agreed:

- There is a strong requirement for a programme of work focused on nuclear data evaluations for charged-particle therapeutic applications.
- Invite representatives of Monte-Carlo code development teams to take part in the programme.

To fulfil these requirements, the Coordinated Research Project (CRP) entitled "Heavy charged-particle interaction data for radiotherapy" began in 2007. The first Research Coordination Meeting (RCM) of the CRP was held at IAEA Headquarters, Vienna, Austria, from 6 to 9 November 2007, and was attended by eleven participants and one observer. The IAEA was represented by A.L. Nichols (Head, Nuclear Data Section), S. Vatnitskiy (NAHU) and R. Capote Noy, who served as Scientific Secretary. H. Paganetti (Massachusetts General Hospital, Boston, USA) was elected Chairman of the meeting; H. Palmans from the National Physical Laboratory, United Kingdom, agreed to act as rapporteur. The approved Agenda is attached (Appendix 1), as well as a list of participants and their affiliations (Appendix 2).

[1] R. Capote and S. Vatnisky, *Summary Report of Consultants' Meeting on "Nuclear Data of Charged-Particle Interactions for Medical Therapy Applications"*, **INDC(NDS)-0504** (IAEA, Vienna, January 2007).

Prior to the meeting, the assignment of tasks following the recommendations of the CM was discussed by e-mail between the participants and Scientific Secretary. The primary aims of this meeting were to discuss scientific and technical matters related to the subject, coordinate related tasks, and to assess assigned responsibilities and deadlines.

Alan Nichols (Head of the IAEA Nuclear Data Section) welcomed the participants, and emphasized the significance of their role in the improvement of the interaction data for radiotherapy applications. R. Capote Noy (IAEA-NDS Project Officer for the CRP) summarized the research objectives and expected outputs of the CRP as outlined in the preceding CM. The following outcomes are expected from the proposed research project:

- Make available experimental and recommended nuclear data parameterisations on the web, recommending new experiments when needed.
- Make available recommended hadronic physics settings for the considered Monte-Carlo codes and applications on the web.
- Publication of a technical document (TRS-level).

The actions to be undertaken prior to the next RCM to be held in the summer of 2009 were agreed; together with their relative time-schedule and deadlines (default deadline for all actions is the next RCM if not explicitly stated). The status of the work, the assigned actions, deadlines and recommendations with regard to the coordinated efforts to be pursued are summarized below.

2. Summary of discussions

A brief overview of experience within the group was given by R. Capote Noy. It was noted that we are missing developers from the MCNP community. R. Capote Noy was requested to address this issue by inviting additional researchers with the desired expertise.

For each of the applications defined during the Consultants' Meeting of 2006[1], the discussions during this meeting have lead to an agreed set of target steps to be followed as well as agreed work packages. These are outlined in the following two sections.

3. Target steps agreed for CRP work

1. Sensitivity analysis based on the table on page 12 of IAEA report **INDC(NDS)-0504** (see also below). But need more refinement e.g in terms of materials/particles. Define the requirements on data for range of applications. Applications need to be extended beyond physics: dose calculations for induction of secondary cancers. How accurate do we need to know each quantity? Quantify contribution of nuclear data to quantity (A. Ferrari: come up with five example exercises on how to asses this).
2. Review data that are available – both experimental and models.
3. What experiments are needed to fill the data gaps?
4. Which data and parameterisations/models are used in MC and how do they refer to experimental data?
5. Review existing benchmarking data and define need for new data (also what experiments are required?). Keep benchmarks as simple as possible. Specify settings per code and application. Two levels of benchmarks: microscopic (L1) and complex cases (but simple geometries L2)
6. Recommend data for various applications and different cases. Recommend MC settings per code and application. To be discussed at the next meeting.

7. Encourage code developers to implement recommended data. To be discussed at the next meeting.

Required steps will be assessed for all applications where nuclear data are of interest. The table from our previous report **(INDC(NDS)-0504)** is reproduced here:

Order on the basis of sensitivity to nuclear data

	Protons	**Ions**
Treatment nozzle simulation and beam characterisation	Total and differential cross-sections for materials of beam shaping devices.	Total and differential cross-sections for incident ions and secondary charged fragments for materials of beam shaping devices.
Primary standards and reference dosimetry	Total and differential cross-sections with high accuracy needed for a limited set of detector materials.	Total and differential cross-sections with high accuracy needed for incident ions, secondary charged fragments, and a limited set of detector materials.
Activation for PET	Production cross-sections for limited set of tissues.	Production cross-sections for incident ions and secondary charged fragments for a limited set of tissues.
Neutron production for protection and shielding	Double differential production cross-sections for tissues, beam shaping devices and shielding materials.	Double differential production cross-sections for incident ions and secondary charged fragments on tissues, beam shaping devices and shielding materials.
Treatment planning dose calculations	Differential production cross-sections for protons and total nonelastic for other charged secondaries.	Differential production cross-sections for incident ions and secondary charged fragments.

4. Contributions from participants per application

4.1. General

Collection of experimental data on nuclear reactions in the context of hadron therapy

N. Sobolevsky: The goal at this stage of the CRP is the collection and compilation of experimental data on the nuclear interaction of protons and light nuclei (up to carbon) with nuclei of chemical elements constituting biological tissue and tissue equivalent materials. Experimental data on nuclear reactions in materials of beam shaping devices are also of interest.

These experimental data are necessary for benchmarking and verification of the transport codes involved in the Project. Currently these codes are MCNP, FLUKA, Geant4, PHITS and SHIELD-HIT.

The energy range of projectiles is approximately limited by the value of 800 MeV for protons and by 400 - 450 MeV/n for carbon beams. While the energy of therapeutic proton beams is limited by ~ 200 MeV, in the case of carbon beams there is high energy tail of secondary nucleons due to nuclear fragmentation up to an energy of roughly twice the primary ion beam

energy in MeV/n. Moreover, the interaction of 400 MeV/n carbon ions with the hydrogen present in tissue is equivalent to the interaction of 400 MeV protons with carbon, e.g. in the viewpoint of PET isotopes production.

Because of nuclear fragmentation of a carbon beam in tissue, the data for all nuclei lighter than carbon (i.e. B, Be, Li, He, D and T) have to be included too.

Chemical elements constituting the biological tissue and tissue equivalent materials, according to the ICRU 37 Report, are the following: ^{1}H, C, N, O, F, Na, Mg, P, S, Cl, K, Ca, Fe and Zn. Elements Al, Cu and Pb should be added for beam shaping devices.

The following types of experimental data on proton-nucleus and nucleus-nucleus interactions are required in order to verify the models of nuclear reactions included in the transport codes:

- Total cross-section and reaction cross-section in absolute units (mb);
- Double differential cross-sections of production of secondary particles (neutrons, protons and nuclear fragments) in absolute units, e.g. mb/(MeV*sr) or mb/((MeV/n)*sr);
- Cross-sections of production of radionuclides – firstly PET-isotopes in absolute units (mb).

Differential/exclusive data are preferable, but integrated data may be acceptable, e.g. energy/angular distributions or charge change cross-sections.

The first step of data collection is formation of the list of bibliographic references with classification by data types (total cross-sections, differential cross-sections, etc.). The next step is extraction of data from original publications and their presentation in plots and tables. Transformation of data to the accepted reference system and kinematics variables may be required.

There is no deadline for data collection. This work continues during the whole duration of the Project. But every 6 months the up to date status of the data should be fixed.

Besides benchmarking of the transport codes, data collection is needed to show gaps in the data and to give recommendations for desirable new experiments.

For each application materials/elements specifications need to be made; define limits in energy range, define what levels of data are required.

Questionnaire

A. Ferrari: A questionnaire will be prepared to review the models, data and parameterizations used in the various codes (6 months). At least a response from five codes is expected (MCNPX, Geant4, SHIELD-HIT, FLUKA and PHITS). If we find others, we will also send them the questionnaire and contact them about activities. The IAEA should provide any relevant information they possess. If code developers are not responsive, we can prepare a second version with proposed answers for them to edit.

- Prepare and circulate within the working group a draft questionnaire (each topic has to be further detailed) for code developers including the following:
    - description of nucleon and ion total reaction and elastic cross-sections used in the codes (data, parameterisations, which parameters, plots, etc.);
    - description of nuclear models both for nucleon- and ion-induced non-elastic reactions;
    - description of models/data used for nuclear elastic scattering;
    - details of nuclear data bases used, and particle/energy range where they apply;

- description of the implementation of relevant atomic physics processes (ionization losses, fluctuations, effective charge, multiple Coulomb scattering and secondary electron production);
- range of application of the models (can exclude large part of data/models)
- suggested settings/models for therapy-related problems;
- existing benchmarks which are of relevance to therapy-related problems.

- Circulate the questionnaire in the developer community once approved (A. Ferrari: 12 months)
- Collect and analyze/organize the answers to the questionnaire (A. Ferrari: 18 months)

4. 2. Treatment head simulation and beam characterisation

4.2.1. Protons

Sensitivity analysis

H. Paganetti: Monte-Carlo codes are being used to help design treatment heads and to characterize treatment fields by producing phase space distributions based on detailed treatment head models. A list of common treatment head materials has to be generated in order to assess the current situation on available experimental data for protons in terms of total and differential cross-sections.

Information has to be collected from different vendors or institutions to identify these materials and elements (C, Cu, O, Al, Zn …). The required data (e.g., total cross-sections or double differential cross-sections) have to be identified. Typically, each of the materials will be exposed over the entire energy range of the beam (0-250 MeV). The importance of double-differential cross-sections may depend on whether these materials are used in either beam shaping or beam modifying devices, and on their typical position in the treatment head.

The sensitivity of physics data with respect to 'typical' applications has to be investigated. For example, what is the impact of brass (aperture) cross-sections on the phase space distributions?

A. Ferrari: Devise 3-4 possible schemes for varying relevant parameters in a (not completely unphysical) manner. For example, variations in cross-sections and in angular distributions, energy distributions and charge distributions of reaction products should be investigated

Check the impact on 2D proton and ion fluence and dose distributions in water of those schemes and reiterate if needed. Check which is the expected nuclear reaction product contribution to proton therapy 2D dose distributions in a water phantom in order to help the definition of suitable sensitivity exercises for protons.

J.M. Quesada: Sensitivity analysis of Geant4 against the different options for (pre-equilibrium) modelling in hadronic physics.

Review of data

H. Paganetti: Data on treatment head simulations and beam characterization from the open literature will be reviewed to identify typical applications, and understand the impact of nuclear data.

Cross-section data for different elements and materials will be collected and reviewed under Section 4.1.

Additional data requirements

H. Paganetti: Additional data requirements will be identified, based on the expected impact of nuclear data ('sensitivity analysis'), the anticipated applications where nuclear data may play a role ('review of data'), and the availability of appropriate cross-sections (Section 1).

Data and parameterisations used in MC codes

A. Ferrari: Prepare and circulate within the working group a draft questionnaire discussed in Section 4.1 above for code developers.

J.M. Quesada: Description of models available in Geant4 for hadronic physics in the energy region of interest in hadron therapy.

- Pre-compound regime:
  - Bertini (own evaporation module is built inside)
  - Binary cascade
  - Pre-compound (exciton)
- Equilibrium regime:
  - Multifragmentation
  - Fermi breakup
  - Fission
  - Evaporation

Benchmark cases

B. Carlson: Calculations (L1 benchmarking) of proton-induced integrated, differential and double-differential cross-sections;

a) Heavy elements (Al, Ca, Ti, Fe, Ni, Cu, Zn, W, Au and Pb) to 250 MeV using exclusive DDHMS + Hauser-Feshbach (Items 1, 2, 4);
b) Light elements (C, N, O, P and Al) to 250 MeV using exclusive DDHMS + fragmentation (Items 3, 5).

R. Capote Noy: calculated data can be compared directly with results of MC on thin targets (intercomparison).

A. Ferrari: If the sensitivity is limited to a specific set of parameters, find 3-4 experimental data sets to perform intercomparisons between MC codes.

J.M. Quesada: Validation (benchmarking) of Geant4 hadronic physics models with thin target (microscopic level) experimental data for secondary neutron emission in proton-induced reactions (test cases already established by the collaboration, as $p+^{27}Al$ @ 22 MeV and $p+^{12}C$ @ 133 MeV, and new ones of special interest for hadrontherapy). Pre-compound and evaporation model implementations are still at development stage (as for multi-fragmentation) and both tasks (validation-development) are obviously correlated.

H. Paganetti: More general benchmarking will be based on multi-layer Faraday cup measurements as described under "Treatment Planning Dose calculations".

4.2.2. Ions

Monte-Carlo codes are being used to help design treatment heads and to characterize the treatment field by producing phase space distributions based on detailed treatment head models. A list of common treatment head materials has to be generated in order to assess the current situation on available experimental data for ions in terms of total and differential cross-sections.

Collection and review of data

(O. Jäkel, K. Henkner, M.C. Morone, N. Sobolevsky, A. Ferrari)

Information has to be collected from different vendors or institutions to identify the materials and elements needed (C, Cu, O, Al, Zn …), exactly as planned for protons (see Section 4.2.1). Typically, each of the materials will be exposed over the entire energy range of the beam. Collected data for ions include attenuation lengths, fragmentation yields, angular distributions, neutron production and reliable depth doses. Experimenters at GSI and HIMAC will be contacted to collect data (agreement will be necessary to use unpublished data within this Project).

As part of the INFN-founded "MOBIDIC" experiment, fragmentation measurements of C ions on different targets will be carried out from 30A to 80A MeV during 2008 (some data could be relevant for beam characterization?)

Sensitivity analysis

The sensitivity of physics data with respect to 'typical' applications has to be investigated. (What is specific for ions?)

Benchmarking

Beam characteristics for MC simulations should be obtained from the analysis of collected data (SHIELD, FLUKA, Geant4, PHITS?)

4.3. Primary standards and reference dosimetry

4.3.1. Protons:

H. Palmans: NPL is developing a graphite calorimeter to serve at primary standard dosimetry level for absorbed dose to water. One of the main uncertainty contributions for this calorimeter is the conversion from absorbed dose to graphite to absorbed dose to water. Nuclear interactions play a major role in this conversion procedure and the uncertainty. Furthermore, nuclear interaction data for the materials of which secondary standard instruments, usually ionization chambers, are composed also contribute to uncertainties in hadron dosimetry through their influence on chamber specific perturbation factors. This project aims to execute a comprehensive set of experiments and Monte-Carlo simulations to reduce the uncertainty in these conversion procedures and ionization chamber perturbation factors.

The proposed work consists of intensive in-phantom measurements in graphite, aluminium, water, PMMA and other materials in proton beams and possibly carbon beams for establishing and understanding the absorbed dose to graphite to absorbed dose to water conversion, including depth doses and tissue phantom ratios using primarily ionization chambers as well as attenuation curves and range measurements using Faraday cups. Monte Carlo simulations of these experiments will be performed using MCNPX and Geant4 (as well as modified versions of PTRAN). In addition, a sensitivity analysis of corrections factors for the calorimeter, such as the gap correction, will be performed by measurements and Monte-Carlo simulations. A similar sensitivity analysis will be performed for ionization chambers which will be compared with the graphite calorimeter using at least two calibration routes to provide additional information for nuclear data validation. Intensive in-phantom measurements in graphite and water will be performed in the Clatterbridge Centre of Oncology (CCO) proton beam in order to establish and understand the absorbed dose to

graphite to absorbed dose to water conversion. These measurements include depth doses and tissue phantom ratios by means of primarily ionization chambers but possibly also diodes and diamonds, as well as attenuation curves and range measurements with Faraday cups. Depending on beam access, similar measurements will be performed in higher-energy proton beams and carbon ion beams. Monte-Carlo simulations of the CCO beam (as well as any other experimental beam line involved) using MCNPX, Geant4 (as well as modified versions of PTRAN) will provide essential data on beam characteristics in the subsequent Monte-Carlo simulation of the experiments by means of the various nuclear data sets and models under validation. Further experiments will be performed to determine the calorimeter gap correction by varying the size of the gap systematically and to quantify relative ionization chamber perturbation factors by comparing various ionization chamber types. These experiments will also be simulated using the same Monte-Carlo codes and various nuclear interaction data and models for validation purposes.

Sensitivity analysis

NPL and collaborators will simulate dose to graphite to dose to water conversion (6 months), total absorption calorimetry experiment (6 months), attenuation experiment using Faraday cup (12 months), graphite calorimeter perturbation corrections (12 months), dose conversions from other materials (e.g. Al), and ion chamber perturbation corrections in protons (18 months) using Geant4 and MCNPX.

H. Palmans to follow up if essential data are missing in above experiments.

Benchmark cases

NPL and collaborators will investigate feasibility of graphite to water conversion experiment (6 months), ion chamber experiment (12 months) and total absorption calorimetry experiment (12 months) as level 2 benchmark cases for phase space description of beam.

4.3.2. Ions

O. Jäkel: Sensitivity analysis of depth dose data (one of the quantities of interest), stopping power ratios, w_{air}-ratio (via all particle contributions, w_{air} being the mean energy required to produce an ion pair in dry air), water calorimetry (experiments in collaboration with PTB to be continued in HIT), and graphite calorimeter (experiments in collaboration with NPL) on the fragment yields and angular distributions performed using SHIELD-HIT (deadline: 6 months)

Benchmark cases

Benchmarking experiments at HIT (data to be published).
Depth dose data. Calorimetry experiment. O. Jäkel pointed out that ion chamber benchmarks require MC tool capable of calculating ionization chamber response, which is not available.
The same systems are basically used for reference dosimetry of ion beams like carbon, namely ionisation chambers and calorimeters (water or solid state). Consequently, the list of materials is the same as specified in Section 4.2.1. The ions of interest for radiotherapy are primarily carbon, but also other ions like helium (^{3}He and ^{4}He), lithium, nitrogen and oxygen are available in some of the new ion therapy facilities and their use for radiotherapy purposes will be investigated in the future. Heavier ions (e.g. neon, silicon and argon) have been used for radiotherapy in Berkeley, but are currently not considered to be useful for radiotherapy application. The use of radioactive beams was investigated in Berkeley (^{11}C) and Himac (^{9}C and ^{11}C), but also seems to be of very limited interest in radiotherapy. These ions are therefore not included in the present study. Since heavy ions undergo mainly projectile fragmentation in

the targets, data for all ions from protons to Oxygen will be needed.

The primary beam energies which are currently available in clinical facilities range from about 50 up to 500MeV/n. Since light secondary particles may have similar energies, the database for all ions has to be available for this energy range. Protons and neutrons from projectile fragmentation may have energies up to twice the primary beam energy (i.e. up to 1 GeV kinetic energy for a primary beam of 500 MeV/n).

The effects of target fragmentation seem to play only a minor role. However, this will be investigated further as part of the sensitivity analysis.

The data needed for investigations in reference dosimetry are accurate depth doses, total fragmentation cross-sections (i.e. fragment yields) and differential cross-sections such as the energy spectra and angular distributions of the produced fragments.

The SHIELD-HIT code was used for investigations of ion chamber dosimetry in Heidelberg, and will be benchmarked against the available data (first benchmark has been performed already by Geithner *et al.*, but inconsistent stopping power data and experimental data have been included). A benchmarking of FLUKA and/or Geant4 against the same data will also be performed in Heidelberg.

The sensitivity of various quantities on the fragmentation yields and differential cross-sections will also be tested. These quantities include the depth dose data, the stopping power ratios of w_{air}-values as calculated from the fragment spectra according to TRS-398. The absolute accuracy of the stopping power and w_{air}-data is not critical, as only the relative variation of the interesting quantities is important for the sensitivity analysis.

In terms of calorimetry for ion beams, the primary goal is to quantify the amount of energy that is not contributing to the heating of the target, i.e. nuclear binding energies and neutrons leaving the sensitive volume. The sensitivity of these simulations on fragment yields will also be investigated. Measurements with water and graphite calorimeters (performed by PTB and possibly NPL, respectively) at the new Heidelberg Ion Beam facility are strongly encouraged.

4.4. Activation for PET

Nuclear data for charged particle therapy monitoring with PET

I. Pshenichnov: Positron-emitting nuclei are produced in human tissues during proton and carbon-ion therapy, and can be used for therapy monitoring. This is usually done by comparing a measured β^+-radioactivity profile with the one calculated for the prescribed dose. The same method can be used with ^{3}He beams or possibly with other light nuclei (e.g. ^{7}Li) as soon as they become available for treatment at new facilities.

Relevant neutron-deficient isotopes which are currently detected in experiments with proton and carbon-ion beams are ^{10}C, ^{11}C, ^{15}O and ^{13}N. They are produced on nuclei of human tissues, ^{12}C, ^{16}O and ^{14}N in nuclear reactions where only a single neutron is lost. In proton and carbon-ion therapy, positron-emitting nuclei are the fragments of target material nuclei or of both beam and target nuclei, respectively. Activity from ^{17}F, ^{18}F and ^{30}P nuclei should be also studied as they can be produced, for example, in bone tissues and by ^{3}He in water.

The total yields of positron emitting nuclei, and hence the total amount of β^+-radioactivity as well as spatial activity profiles is extremely sensitive to nuclear data. The total β^+-

radioactivity profile which is built through the contributions of specific radioactive nuclei changes with time as these isotopes have different half-lives and their production rates vary with depth in tissues. In summary, reliable computational tools which are based on or validated with nuclear reaction data are necessary in order to implement the PET monitoring technique in charged-particle therapy.

First 6 to 12 months:

Preliminary sensitivity study: calculate variations of total β^+-radioactivity profiles due to variations in the contributions of individual isotopes for several beam energies and tissue-like materials. This study should be done for various measurement time windows on- and off-line as well as for various spatial resolutions of the PET scanner. Compare the estimated uncertainties with typical uncertainties in nuclear data for the most crucial contributors to β^+-radioactivity (most important or most uncertain).

Review data: compile the list of measurements of excitation functions for ^{10}C, ^{11}C, ^{15}O, ^{13}N and others. Compare the content of IAEA/NEA databases (including dedicated medical radionuclide production: http://www-nds.iaea.org/radionuclides/) with the ISI Thomson Scientific and other bibliographic resources. Suggest data for inclusion in IAEA/NEA databases. Try to include thick target yields in the analysis and check the consistency of collected data. Underline the most robust experimental results with minimal uncertainties.

From 6 to 18 months:

Calculations: Compare selected data with Geant4 results on isotope production for thin and thick targets obtained with several hadronic models of the toolkit. Find the most crucial deviations from the isotope production data taking into account experimental uncertainties. Try to identify the best set of models and their corresponding parameters. Re-check the accuracy of dose calculations with the models considered. Provide a list of requirements from Geant4 users in particle therapy to be conveyed to Geant4 developers.

Provide recommendations for new measurements: Identify which data are necessary for the most crucial tests of the Geant4 models. Calculate for the proposed cases and make predictions to be tested with proton and carbon-ion beams as well as with beams of lighter ions.

O. Jäkel: The first action will be the collection of all available experimental data relevant to the production of β^+-emitters in light ion induced reactions on isotopes present in tissue. Microscopic data for ^{18}F, ^{15}O, ^{13}N, ^{11}C, ^{10}C, etc. production in reactions induced by ^3He, Li, carbon and oxygen ions in the energy range from the Coulomb barrier up to 500 MeV/n will be of interest.

Excitation functions for β^+-emitter production by protons (see the previous paragraph) will also be of relevance since hydrogen is a component of human tissues. Experimental data for ion-induced production will be possibly found in the Heilbronn/Nakamura compilation. Most available data are anticipated to be at low energies. New experimental data for carbon up to 80 MeV/n should become available in the near future thanks to measurements at the Laboratori Nazionali del Sud, Catania, Italy.

Data measured at GSI with PET scanners by the Rossendorf group during and after ion beam irradiations of water, PMMA and graphite phantoms will also be collected and made available for comparisons (K. Parodi, HIT, and F. Sommerer, CERN, will be contacted for this purpose). Those data have been taken at energies relevant for therapy and will represent a

stringent check, albeit an integral one on the ability of the various models/codes to produce the measured integral and spatial distributions of β^+-emitters. Data should be available for ^{3}He, Li, ^{12}C and ^{16}O ion beams: relevant benchmarks will be defined with the help of K. Parodi, F. Sommerer and the Rossendorf group. Data collection should be completed within 12 months, and the benchmark definition should be finalized at the next meeting. IAEA is willing to compile and format the collected microscopic data and insert them into EXFOR.

Suitable end points for online and offline therapy PET monitoring will be defined: at present, the anticipated aim is for the sensitivity analysis to be carried out for range monitoring with PET.

Benchmarks

A. Ferrari, I. Pshenichnov and O. Jäkel.

4.5. Neutron production for protection

H. Paganetti and A. Ferrari will determine the set of materials/elements typically used in proton and ion therapy treatment heads and define the energy limits for possible interactions with these materials. H. Paganetti will investigate the contribution of nuclear interactions (i.e. cross-section data) from these materials to any information sensitive to treatment head simulations (e.g. phase space calculations, fluence reduction, 'scattered' radiation) (6 months).

H. Paganetti will study the sensitivity of different neutron data (or model settings) on dose, neutron energy distributions, and equivalent dose (using the ICRP92 definition for the radiation weighting factor). He will also compare MGH data on Bonner sphere measurements and microdosimetric measurements with Geant4 Monte-Carlo simulations based on the reference physics list. There is a possible link to the sensitivity analysis, using different global (not material-specific) physics settings (12 months).

Data collection will be coordinated by N. Sobolevsky, who will also search and collect relevant experimental data, especially from Russian journals and pre-prints (both bibliographic references and data will be extracted). R. Capote Noy, B. Carlson, A. Ferrari and O. Jäkel will also contribute to the collection of experimental data from thin and stopping targets, and check for differences between published data and the database (6 months).

R. Capote Noy will oversee compilation into the EXFOR database of relevant experimental data for proton- and carbon-induced reactions as communicated by participants or as they become available.

R. Capote Noy will review available reaction cross-section parameterizations for neutron- and charged-particle-induced reactions up to ~ 200 MeV (relevant for statistical models), and exchange information with MC developers (6 months).

R. Capote Noy and B. Carlson will compare available evaluated data files for proton-induced reactions (LA-150, JENDL, JEFF 3.1 or ENDF-B/VII) with the experimental data. They will also produce theoretical calculations of proton-induced reactions by means of the EMPIRE nuclear-reaction system, and compare with the available evaluated and experimental data up to 250 MeV incident energy, with special emphasis on total reaction cross-sections, neutron and proton emissions and selected double-differential cross-sections (12-18 months).

A. Ferrari will produce theoretical calculations of proton- and ion-induced reactions using

FLUKA, and compare with the available experimental data, with special emphasis on total reaction cross-sections, neutron and proton emissions and selected double-differential cross-sections (12-18 months).

J.M. Quesada will produce theoretical calculations of proton- and ion-induced reactions by means of Geant4, and compare with the available experimental data, with special emphasis on total reaction cross-sections, neutron and proton emissions and selected double-differential cross-sections (12-18 months)

K. Niita will produce theoretical calculations of ion-induced reactions by means of PHITS, and compare with the available experimental data, with special emphasis on total reaction cross-sections, neutron and proton emissions and selected double-differential cross-sections (12-18 months).

R. Capote Noy, B. Carlson, A. Ferrari, J.M. Quesada and K. Niita will perform an intercomparison of their reaction calculations.

Benchmarks

Need to be defined, e.g. total absorption calorimetry experiment, Bonner spheres experiments, Ring experiment CERN?

4.6. Treatment planning dose calculations

4.6.1. Protons:

H. Paganetti:

Data collection for protons and ions

Published total and differential cross-sections for human tissue materials/elements have to be identified. Goal is to investigate the contribution of nuclear interactions (i.e. cross-section data) from these materials to the dose when undertaking Monte-Carlo dose calculation in patient geometries (6 months).

Sensitivity analysis

The sensitivity of the nuclear data in terms of dose distributions in the patient will be determined on the basis of dose calculations in the patient (using treatment head phase space distributions) undertaken by Geant4. Simulations for different field parameters (i.e. beam energies) and different geometries (head and neck with bony structures versus soft tissue cases) will be applied to study the contribution of nuclear interaction products (secondary protons) to the dose distribution (12 months).

Identify experimental data required to fill gaps

Based on the assessment of existing experimental data and the sensitivity analysis given above, one has to define required experimental data to fill gaps in cross-section or model data (18 months).

Benchmarks

The Geant4 Monte-Carlo calculations and associated physics settings will be benchmarked against experimental data from multi-layer Faraday cup (MLFC) experiments carried out at the Harvard Cyclotron Laboratory (experimental data have already been published). The data will be provided to users of other codes (MCNPX, SHIELD-HIT, FLUKA) in order to run similar comparisons. Depending on the availability of the treatment rooms at MGH for

measurements, additional experiments with the MLFC will be performed using pencil beams of different beam energies. If possible, pristine peaks with small energy spread will be used in order to be independent of Monte-Carlo generated phase space data (may only be possible with some computational approximations regarding the MGH treatment head settings). B. Gottschalk (HIT, Heidelberg) will be contacted to determine the status of the MLFC devices, which have not been used for many years. Additional experiments could involve large fields in order to detect lateral particle loss for comparison with the Monte-Carlo prediction. A possible shortcoming is that this study would have to be based on Monte-Carlo simulated treatment head phase spaces because of the use of a double-scattering system to produce a broad beam (18 months).

A. Lomax:

The overall aim of this work package is to assess the sensitivity of complex proton fields and geometries to changes in the data and/or parameterisations used by MC codes to model nuclear interactions effects. As such, we propose to take advantage of the database of IMPT (Intensity Modulated Proton Therapy) already delivered and verified at PSI. As part of the verification process of these fields, variations of a few % have been found between measurement and calculation, particularly in low dose 'valleys' (overdosage) and high dose 'peaks' (underdosage). This observation has been attributed to a secondary proton 'halo' around the primary proton distribution, which has subsequently been modelled by means of an analytical approach (two Gaussians approximation) by Pedroni *et al.* (2003). Using this model, good agreement can be found between measurement and calculation in homogenous phantoms, and we propose that this effect could be a good benchmark for assessing the sensitivity of calculated MC dose distributions to the accuracy of nuclear interaction data sets or models.

We propose the following approach in order to assess the sensitivity of treatment planning dose distributions to controlled changes in the cross-sectional data:

- Implementation of PSI spot scanning delivery in the MGH Geant4 MC package. A large available database of patient plans can then be exploited.
- Assessment of dose 'halo' for geometric distributions in homogenous media, and comparison between analytic (EP model: 2-Gaussian for primary, one for secondary) and MC code. Frame experiment as benchmark, and extended in terms of phantoms and target shapes.
- Application of MC calculations to clinical IMPT fields, both in patient and homogenous phantoms, and compare MC results for clinical fields with verification (IC) measurements.
- Assessment of variation in results as function of 'modulated' nuclear cross-section data (scaling factors?)
- Definition of definitive 'benchmark' experiment (with measured data) for publication in final report.

1. Implementation of PSI spot scanning delivery in the MGH Geant4 MC package (6 months).

A clinical IMPT database only exists at PSI, whereas the only 'full physics' MC package that supports both geometric phantoms as well as full resolution CT data sets of patients is only available at MGH. For this sensitivity analysis, an interface must first be defined whereby the beam data and field descriptions of IMPT plans (stored either in DICOM or PSI in-house formats) can be imported into the Geant4-based package of MGH. This definition will be the first step in this work package. A QA process will then be developed in order to check that the MC implementation of PSI pencil beams and fields (phantom and clinical) matches that of the

analytical calculation (in homogenous cases only).

2. Assessment of dose 'halo' in geometric distributions in homogenous media, and comparison between analytic (EP model) and MC code (6 months).

After ascertaining a correspondence between the MC and analytical systems in the homogenous case, a series of geometric dose distributions will be calculated using the PSI planning system, designed to allow for the analysis of the effects of nuclear interaction effects. Possible examples will be square frames or circular doughnut-shaped fields, in which the interior hole and outer ring width can be varied. Analysis of these results (from the analytical and MC calculations) will be compared, primarily by analyzing the dose distributions in the interior hole where we expect the distribution to be quite sensitive to the yield and angular distribution of secondary protons generated in the primary dose 'ring' distribution. An alternative approach would be to look at the 'frame' experiments already performed for the parameterization of the analytical approach of Pedroni *et al.* As necessary, measurements of these geometric fields could be performed at PSI as the 'gold standard' for the benchmarking exercise.

3. Application of MC calculations to clinical IMPT fields, both in patient and homogenous phantoms and comparison of MC results for clinical fields against verification (IC) measurements (12 months).

The above methods will be extended to the recalculation of clinical IMPT fields in the MC package. This work will be performed both in the patient CT data sets, and in homogenous 'verification' phantoms (homogenous water phantoms). For the first case, sensitivity analysis can be used to give the 'true' clinical condition (i.e. clinical dose distributions calculated in patient geometry), while for the second cases the MC calculated distributions can be directly compared with the IC-based verification measurements performed for every applied IMPT field. This approach will help validate the MC for this IMPT implementation, and will provide a measurement-based benchmark against which the sensitivity analysis can be ultimately compared.

4. Assessment of variation in results as function of 'modulated' nuclear cross-section data (12 months).

As part of topics 2 and 3 above, the various parameters of the nuclear interaction data or models will be varied and compared with the analytical and measured data to ascertain the sensitivity of the resulting dose distributions to these variations, and how they compare with the measured data.

5. Definition of definitive 'benchmark' experiment (with measured data) for publication in final report (18 months).

We propose that one or two of the geometric distributions developed for the sensitivity analysis described in 2-4 above could also be used to define benchmark distributions against which other MC packages can compare their modelling of nuclear data sets with the measured data of PSI. We believe that defining a benchmark based on pencil beam scanning in simple geometric phantoms makes for a relatively simple parameterization of the beam characteristics (no need to model the whole delivery nozzle) and a simple simulation of the benchmark. Additionally, this benchmark can be directly related to simple (and hopefully robust) measurements that will necessarily be sensitive to changes in the halo distribution. This work will be a constituent of a more comprehensive benchmarking protocol defined separately in this report (e.g. modelling and simulation in a multi-leaf Faraday cup).

A. Ferrari:

See details in Section 4.2. Deadlines are defined below.
Definition of sensitivity parameters (6-12 months).
Initial sensitivity check on proton fluencies (12 months).
Check of sensitivity of dose distributions in homogenous phantoms (6 months).

N. Sobolevsky:

Sensitivity study in terms of dose by means of the SHIELD-HIT code.
Benchmarks of transverse dose distribution, depth dose distribution and fluence distribution.
Summarize the parameter setting of the SHIELD-HIT calculations.

M.C. Morone:

Use of FLUKA for benchmarking of proton distributions as soon as "benchmark data" are defined.

4.6.2. Ions:

H. Paganetti:

Treatment Planning Dose Calculations benchmarks

There is the possibility to use the MLFC devices in carbon ion beams at HIT, Heidelberg (contact Bernie Gottschalk to determine status of device and possible use). O. Jäkel will perform simulations to investigate whether such measuremernts can produce valuable information (6 months).

However, because of the many different reaction channels in carbon ion nuclear interactions (including fragmentation), the use of the device as a benchmarking tool may not be as valuable as in the case of protons. B. Gottschalk (HIT, Heidelberg) has to be contacted to determine whether the device can be shipped, if the electronic readout system can be purchased off the shelf, or has to be the specific device developed in-house at Harvard. Further, if B. Gottschalk agrees that the device can be used outside of MGH, we need to clarify whether he has to be involved personally and how this can be accomplished/funded (6 months).

O. Jäkel, K. Henkner:

General: collecting data such as attenuation lengths, fragmentation yields, angular distributions, neutron production, reliable depth doses (not always clear from experimental data) and contact experimenters at GSI and HIMAC (including unpublished data + agreement to use them).

Discussion: energy derivation from range (ambiguity uncomfortable for MC users/developers).

Benchmarking for SHIELD-HIT against these data (partly done by O. Geitner, and continued by K. Henkner and N. Bassler).

Consider experiment with MLFC at HIT or GSI (test sensitivity first!), also possibly protons (very clean beam) to provide beam characteristics and phase space.

Treatment planning dose calculations

Sensitivity of depth dose, SOBP in water, lateral penumbra and simple plans (for

heterogeneous phantoms including bone/tissue and tissue/air interfaces) on the fragment yields and angular distributions, e.g. frame experiment including larger depths.

Sensitivity of fragment yield on target composition/tissue, e.g. bone. Sensitivity of RBE in monoenergetic and SOBP case on fragment yields and in lateral penumbra (on the angular distributions?)

Benchmark experiments for phantom geometries.

A. Ferrari:

Sensitivity analysis

See details in Section 4.2. Deadlines are defined below. Activities are the same both for protons and ions.

Contribute to data collection/selection (6 months).
Definition of sensitivity parameters (6-12 months).
Initial sensitivity check on ion fluencies (12 months).
Check of sensitivity of dose distributions in homogenous phantoms (6 months).

Review of models, data and parameterizations used in the various codes:
Prepare and circulate within the working group a draft questionnaire discussed in Section 4.1 above for code developers.

Ion fragmentation:

Contribution to data collection and definition of first level benchmarks (12 months).
Run first level benchmarks with FLUKA (18 months).
Run second level benchmarks with FLUKA (24++ months).

R. Capote Noy noted that we should have all benchmarks defined by the next meeting. L1 are relatively easy to set up and run; L2 need to be started in a timely manner.

M.C. Morone:

Treatment planning dose calculation

Review/collect experimental data relative to reactions of carbon ions in the energy range of interest for hadron therapy.

Benchmarks

Run FLUKA on benchmark data for C ions and protons as soon as “benchmark data” have been defined.

Measurements

As part of the INFN-founded “MOBIDIC” experiment, fragmentation measurements of C ions on different targets will be carried out from 30A to 80A MeV during 2008. Contribute to data accumulation and analysis, prior to release in 2009. Hopefully, these data will constitute a benchmark for MC codes.

K. Niita:

Sensitivity study in terms of dose by means of the PHITS code

Benchmarks of transverse dose distribution, depth dose distribution and fluence distribution.

Summarize the parameter setting of the PHITS calculations, and provide input files for these benchmarks

5. PROJECT WEB SITE

A project area has been established on the NDS server running under the Linux operating system for exchange of information. Accessible as http://www-nds.iaea.org/charpar/

6. CONCLUSIONS

Presentations and discussions during the meeting showed that there is an agreed consensus concerning the tasks required for the CRP. Furthermore, by discussing the various issues related to the nuclear data, detailed planning of the tasks in general and for each member of the group was accomplished. Issues related to data collection and compilation, sensitivity studies, benchmarks and dosimetry for both proton and heavy-ion radiotherapy were extensively debated. The main goals to be achieved within the project and expected outcomes were clearly defined. Further extensive work needs to be done in the next 15 months so that the necessary progress can be achieved before the next RCM. A truly coordinated programme of work was agreed among the participants, leading to several additional actions that need to be undertaken.

The next Research Coordination Meeting will be held in the second half of June, or the first half of July 2009 in Seville, Spain.

IAEA
Atoms for Peace: The First Half Century
1957–2007

1st Research Coordination Meeting on

"Heavy charged-particle interaction data for radiotherapy"

IAEA Headquarters, Vienna, Austria, 6 – 9 November 2007
Meeting Room A2313

AGENDA

Tuesday, 6 November

08:30 - 09:30	**Registration** (IAEA Registration desk, Gate 1)
09:30 - 10:00	**Opening Session**
	Welcoming address – Pedro Andreo
	Introductory Remarks – Roberto Capote Noy
	Election of Chairman and Rapporteur
	Adoption of Agenda
10:00 - 10:45	**Administrative and Financial Matters related to participants**
	Coffee break
10:45 - 12:30	**Session 1: Discussion of Research Proposals**
12:30 – 14:00	**Lunch**
14:00 – 18:00	**Session 1 (cont'd): Discussion of Research Proposals**
	Coffee break (as needed)

Wednesday, 7 November

09:00 - 12:30	**Session 1 (cont'd): Discussion of Research Proposals**
	Coffee break (as needed)
12:30 - 14:00	**Lunch**
14:00 – 18:00	**Session 1 (cont'd): Discussion of Research Proposals**
	Coffee break (as needed)
19:00	**Dinner at a restaurant in the city**

Thursday, 8 November

09:00 - 12:30	**Session 2: Discussion of the expected outputs**
	Coffee break (as needed)
12:30 - 14:00	**Lunch**
14:00 – 18:00	**Session 2: Discussion of the expected outputs**
	Coffee break (as needed)

Friday, 9 November

09:00 - 12:30	**Drafting of the Summary Report of the Meeting**
	Coffee break (as needed)
12:30 - 14:00	**Lunch**
14:00 – 17:30	**Review and Approval of the Summary Report**
	Closing of the Meeting

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