

Dr. Steve Myers Head of CERN Medical Applications Former Director of Accelerators and Technology CERN DG/DI 1211 Geneva 23. Switzerland

 Tel. direct:
 + 41 (0)22 767 3406

 Tel. secretariat
 + 41 (0)22 767 5743

 Email:
 steve.myers@cern.ch

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Letter to Participants of Divonne 2014

Geneva, 19th February, 2015

Dear Colleagues,

I realised recently that it is one year since we had our kick-off meeting in Divonne near Geneva. The next Divonne meeting will be following ICTR-PHE 2016 and will be held in Divonne from 4<sup>th</sup> evening to 6<sup>th</sup> lunch March 2016.

I also realise that there has been little communication on our progress during the last year. For this reason I am writing this "annual progress report" to all participants of Divonne 2014.

# Introduction

Since our meeting in February last year we have made excellent progress in some fields whereas the headway in other domains has been mediocre. In what follows I will try to give some insight to the evolution we have on the following subjects:

- Administration and legal issues;
- Funding;
- Technical issues;
- Dissemination of information.

Firstly, I should give you a short reminder of the outcome of the discussions at Divonne.

"In January 2014, the CERN Director General created an Office for Medical Applications (OMA), and planned provision of "seed" resources (manpower and funding) to allow further development of this Office by collaboration with other institutes. The remit for the new Office is to apply the three CERN key technologies (particle detectors, large scale computing and particle accelerators) to the field of medicine. This enterprise consists of **seven** initiatives related to medicine and medical research:

- Large Scale Computing for data storage, transfer and analysis; bio-medical simulations and treatment planning,
- Detectors for medical imaging using recently developed particle physics technologies,

- Radio-Isotopes for bio-marking, imaging and treatment; using the ISOLDE facility,
- New Biomedical Facility OPENMED
  - creation of a facility, using the existing Low Energy Ion Ring (LEIR), that provides particle beams of different types and energies to external users for radiobiology experiments, as well as acts as a test-bed for medical detector development, and for iterative experimental verification of biomedical simulations,
- Medical Accelerator Design
  - coordinate an international collaboration to design a new compact, costeffective accelerator facility, using recently developed technologies
- Physical and Biological Modelling, Diagnostics and Dosimetry for radiation control during treatment
- Applications other than cancer therapy."

# Administrative and Legal Progress

The structure for the Office has been decided and several internal and external collaboration boards and committees have been set up. Some external funding has already been donated and many more avenues are being explored for additional funding.

We have now successfully merged the 7 different medical initiative entities into one framework without disrupting their previous positive progress.

Following the "Divonne" meeting, an internal CERN Medical Applications Study Group (CMASG) has been set up with representatives from the seven initiatives (see Figure 1). The CMASG meets on a bi-weekly basis and discusses the medical initiatives with emphasis on interaction and synergies between the initiatives.



Figure 1 Draft structure of the Office for Medical Applications

In summer 2014 we created an International Strategy Committee (ISC), with members from major institutes in Europe, USA, China and Japan (see Table 1 for a list of members and advisors). The first meeting was held at CERN on 20/21 November 2014 and the second is foreseen in Brussels in April 2015. During the first ISC meeting the strategy for the medical initiatives was discussed at length and endorsed by the committee. A commitment was also made by the committee members to lobby for funding for the most important and urgent projects.

Surnamo	First Name	Instituto	Country	Speciality
Juinanie	First Name		country	speciality
Amaldi	Ugo	TERA	Italy	Physics
Baumann	Michael	Dresden	Germany	Radiobiology/oncology
Debus	Jurgen	HIT	Germany	Physics
Del Guerra	Alberto	Uni Pisa	Italy	Physics
Dosanjh	Manjit	CERN	Switzerland	biology
Durante	Marco	GSI	Germany	Radiobiology
Hausterman	Karin	Leuven	Belgium	Radio-oncology
Jones	Bleddyn	Oxford	UK	Scientific secretary
Lambin	Philippe	Maastro	Netherland	Medicine
Lewensohn	Rolf	Karolinska	Sweden	Physics
Mayer	Ramona	Med-austron	Austria	Radio-oncology
Mazal	Alejandro	Institut Curie	France	Physics
Mohan	Radhe	MDAnderson	USA	Radio-oncology
Myers	Stephen	CERN	Switzerland	Accelerators
Orecchia	Roberto	CNAO	Italy	Medicine
Overgaard	Jens	Aarhus	Denmark	Radio-oncology
Poetter	Richard	Vienna	Austria	Senior Advisor
Prior	John	CHUV	Switzerland	Radio-oncology
Prise	Kevin	QUB	UK	Radiobiology
Schippers	Marco	PSI	Switzerland	Physics
Townsend	David	NUHS	Singapore	Physics
Tsujii	Hirohiko	NIRS	Japan	Radio-oncology
Vikram	Bhadrasain	NIH	USA	Senior Advisor
Waligorski	Mike	INP, Krakow	Poland	Physics
Zhang	Shen	Shanghai	China	Medicine

Table 1: Members of the International Strategy Committee:

M. Baumann is the medical chair, S. Myers chairs the physics part,

R. Poetter, B. Vikram are senior scientific advisors, and B. Jones the scientific secretary.

The proposed draft structure of the OMA is given in Figure 1 with ticks indicating where the necessary actions have been completed. Clearly, one important action for 2015 is the setting up of the "international collaboration board". This has already been initiated and discussions with around 6 countries have taken place. The goal is to finalize the composition and remit of this board by the end of 2015.

Where progress has been slow, is in the search for an efficient governance for the ensemble of our activities. At present, the legal status and the governance of the Medical Applications Office is being studied by the CERN Legal service and a proposal will soon be presented to the CERN Council for endorsement. Following this endorsement, Memoranda of Understanding and Collaboration-Partnership Agreements will soon be available.

#### **Progress in Funding**

The "seed" funding from CERN amounts to a total of 2MCHF per year for at least the next 5 years. This budget line is included in the 5-year CERN Medium Term Plan which was approved by the Council in June 2014. The total funding is equally split between materials and personnel (1MCHF/year for each). It is evident that we will need substantial additional external funding in order to make progress with our projects.

During 2014 and the first part of 2015 we have been actively exploring funding possibilities with various funding agencies, non-profit making foundations and the EC. One of our main focuses has been on the EC Horizon 2020 programme. Until now we have not been successful in securing substantial funds for our programme.

On a more positive note, we have received a donation of 1MCHF towards the budget of the OMA from a commercial company. The first slice of this donation has been transferred via the new CERN and Society Foundation. This foundation is also actively searching funding for the OMA.

Recently, we have submitted a joint proposal with 10 partners for a "Distributed Data for Decision support and Learning as a Virtual Environment (D3LVE)" with CERN contributing usage of the LHC grid and data analysis tools developed for particle physics. This proposal was initiated by Philippe Lambin (Maastro) end of November 2014, was submitted on January 14 and will be coordinated by CERN. We shall receive the results by May-June 2015. Our top priority for funding is OPENMED, the conversion of LEIR to a bio-medical test facility at CERN. Our proposals to the Wellcome trust and the EC have been unsuccessful. Following the recent visits of dignitaries from the EC, we will prepare a new EC proposal for consideration in June 2015.

In early 2015, we have had meetings at CERN with the outgoing and incoming commissioners for Research and Innovation with follow up meetings in Brussels. We have also had regular contact with the EC Director General of Research, Health and Innovation as well as with the Directors of Health, Infrastructures and Computing. We are still searching for the correct funding vehicles for each of our initiatives. During these meetings in early 2015 we were informed of a new call associated with a proposal from the new President of the European Commission ("Juncker's call"). We are starting to prepare for a number of funding calls for several of our development pursuits: RFQ, medical imaging, large data, and OPENMED.

#### **Technical Progress**

# High Frequency RFQ

At the beginning of 2014, our limited CERN materials funds were concentrated on the development of a high frequency RFQ to serve as a pre-injector for a hadron therapy accelerator. Since then, considerable progress has been made and a prototype operating at 750MHz will be constructed by the end of 2015. It has become apparent that this HF RFQ enhanced with upgrades and some accelerating modules may also be a candidate for the

production of radio-isotopes for PET scanners as well as the production of 99m-Technetium. Consequently, the HF RFQ has become a very attractive piece of equipment for manufacture by commercial companies.

#### MEDICIS

On the production of medical radio-isotopes; the MEDICIS building has been completed and some additional funding is now being searched to allow operation with light targets to start in 2016. A cost and schedule review of the MEDICIS project is foreseen for spring 2015. I have been invited to chair this review.

MEDICIS has been successful in obtaining funding from the EC via a Marie-Curie Training network (funded by Horizon 2020) to train young scientists in the required disciplines and to complete the MEDICIS program with the post-acceleration of 11Carbon PET isotopes for hadron therapy.

#### Large Scale Computing and Data Handling

A proposal for EC funding has been submitted on January 14, 2015 called Distributed Data for Decision support and Learning as a Virtual Environment (D3LVE). This proposal involves 11 participants; CERN (coordinator), Maastro Clinic, UNI Amsterdam, Sohard Software, Catholic University of Rome, ptTheragnostic BV, ELearning4Health BV, NUIG Galway-Ireland, GNUBILA, German Cancer Consortium, University of Oxford. This proposal was initiated by Ph. Lambin during the first International Strategy Committee meeting.

In addition, there have been proposals from the US NCI as well as University Hospitals in the Geneva region to apply the data handling tools developed for the LHC to medical data. The governance of this data (confidentiality and anonymity) is a hurdle which must be overcome before we can make a CERN commitment. It should be noted that the required tools already exist at CERN.

We have also organized a joint meeting between the IT OPENIab group and the medical applications office. This resulted in a workshop to define the IT requirements for the CERN medical initiatives.

#### Medical Simulations and Treatment Planning

The FLUKA Monte Carlo code has been extensively used at HIT and CNAO for the generation of the physical databases for the Treatment Planning Systems TPS in use in these centres. It is also used for verification and sometimes further optimization of the treatment plans computed with the analytical TPS. Future research is focused on the development of an easy-to-use MC treatment planning system for radiation therapy, which is able to calculate conventional proton and ion (from 3He up to 16O) treatment plans for single and multiple fields coupled with different imaging techniques taking into account several different radio-biological models.

The proposed MC based TP system will be interfaced with different image modalities, but use the standard computer tomography (CT) images as the basic requirement. They will calculate

run-time dose/RBE-weighted dose distributions together with PET and prompt photons/particles emission allowing for a verification "in the clinic" of the treatment delivery (in-beam, in-room and offline).

# **Detectors for Medical Imaging**

Several multinational collaborative projects involving medical groups and industries have already been initiated by the HEP community. In particular, we note the Medipix and the Crystal Clear collaboration (CERN experiment RD18) (ClearPET, ClearPEM, ClearPEM-Sonic, BrainPET, EndoTOFPET-US, TURBOPET, ERC-TICAL, PICOSEC, FAST, Penelope, etc.); with several of them having been funded by the European Commission.

# New Biomedical Facility OPENMED

The analyses and design of the technical modifications needed to convert the Low Energy Ion Ring (LEIR) into an accelerator for bio-medical research are very well advanced. The studies of the new injection and extraction systems as well as the modifications for the accelerator lattice are at an advanced stage and waiting for funding. The bio-medical "end-station" study will be initiated during 2015 in collaboration with medical experts since CERN has no expertise in this field.

# Medical Accelerator Design

Progress here is limited to considerations of user specifications of a future facility. The considerations for an "ideal" facility require further study on affordability, size, cost-effectiveness, requirements on beam parameters (type of particle, rate of change of beam energy, ...), beam distribution (gantry etc.), diagnostics, real-time imaging and dose measurement, and the type of accelerator (synctrotron, linac, cyclotron or a combination). Agreement on these specifications will influence the design of a future hadron accelerator for cancer therapy as will the outcome of the experiments on OPENMED.

# Applications other than cancer therapy

This is a relatively new topic and still technically at the early stages of brainstorming. It is foreseen that a special kick-off workshop will be organised during one of the large established medical conferences.

# **Dissemination**

# White paper

A vision white paper is at the final stages of editing. It is foreseen that this paper will be produced in a popular form for non-specialists so that it can be distributed to all interested parties including the general public and funding agencies.

#### WEB site

In order to improve our communication we are setting up a WEB site on medical applications. Progress is well advanced here and the site should go public around March 2015. We foresee that all information relative to the CERN Office for Medical applications can be easily found on this site. Of course this report, the white paper, funding news etc. will all be posted on this new site.

#### **Public Seminars**

We have introduced a new series of public seminars on medical applications entitled "Accelerating Medicine". So far we have had three seminars with presentations by most distinguished lecturers.

#### Collaborations

We have had a host of requests for collaborations. It is impossible to mention all of them here, but the more advanced proposals are from Greece, S. Korea, the University of Texas, NCI, the University of Toronto, the QATAR foundation, Geneva and Lausanne Hospitals, etc.

Best Wishes,

Steve Myers