

Report: Lars Nyvang's visit at the Memorial Sloan-Kettering Cancer Centre (MSKCC), New York

Introduction

I visited the Memorial Sloan-Kettering Cancer Centre in New York from the 8th of February to the 12th of February 2010. I am very grateful to Varian as well as the award board of NACP without who I would never have received the grant.

Background

Almost all radiotherapy centres use photons as the preferred modality for treatment of cancer. Other modalities could be protons or heavy ions such as carbon. There are several good reasons for not (yet) using heavy ions for therapy on a larger scale, one of them is the price for the facility, another is the lack of experience and knowledge in the area of particle therapy. A few centres in the world do however offer patients treatment with carbon ions which is our main interest in this project. One of the most modern and 'state of the art facilities' to deliver radiotherapy with carbon ions is HIT¹ (Heidelberger Ionenstrahl-Therapie) in Germany. We have established collaboration with researchers in Heidelberg through whom we have gained access to their computational resources making us able to do physical as well as biological dose calculations. The calculations are based on the TRiP98² code [3], which has been under development ever since at least 2000. TRiP includes the enhanced relative biological effectiveness (RBE) of carbon ions in a biological optimization.

The idea of this project is to compare different kinds of strategies to boost hypoxic regions of a tumour, exploring treatment planning (dose painting) studies with different modalities and techniques such as RapidArc, IMRT, IMPT and carbon ions (IMCIT). The planning studies will be based on CT and PET images acquired in Aarhus, with F-MISO and FAZA used as a surrogate marker of hypoxia. The proton treatment planning studies are performed using Eclipse (stand-alone research system) whereas the planning studies with carbon ions are made possible due to our cooperation with DKFZ and HIT in Heidelberg as mentioned above.

It is well known that the level of oxygenation of a tumour not only in head and neck cancer [2] but also for other treatment sites is an important parameter for the outcome after treatment with radiotherapy. In tumours irradiated with photons with volumes being hypoxic a higher dose is needed to achieve the same biological outcome as you would have had in a fully oxygenated tumour. This is expressed in the oxygen enhancement ratio (OER), which is in the order of 3 for photons. Giving a dose which is increased with a factor of three will increase the dose to critical structures with a factor of three as well. In many cases this will not be tolerable. For a OER of 1,5 as is the case for carbon ions the situation is completely different, also considering modern techniques such as spot scanning to create highly conformal dose distributions. Figure 1-4 below give an indication of the different dose distributions achievable when radiation modality is changed.

¹ HIT opened November 2nd 2009 and has thus begun to treat patients.

² TRiP is an abbreviation of **T**reatment **p**lann**I**ng for **P**articles.

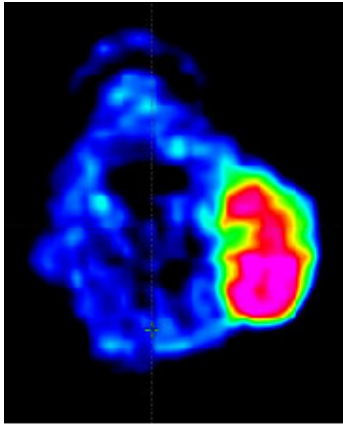


Figure 1: PET image, F-MISO

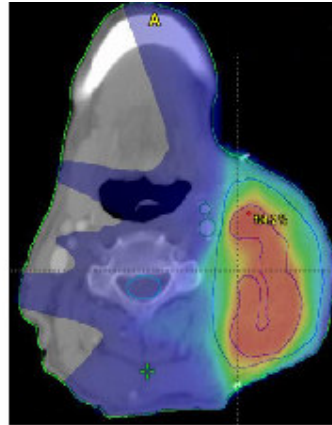


Figure 2: IMRT-boost

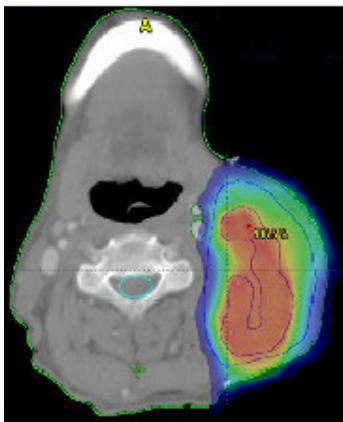


Figure 3: IMPT-boost
(protons)

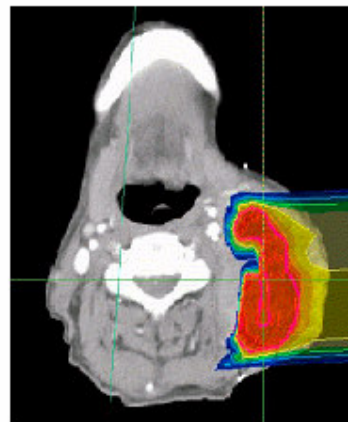


Figure 4: IMCIT-boost
(carbon ions)

Hopefully parts of this work will contribute to development of joint clinical trials together with DKFZ. The outcome of this project is depending heavily on our ability to plan with RapidArc as well as protons, and of our understanding of the concept of dose painting based on imaging of hypoxic regions.

The idea of dose painting is not new. Clifton Ling and co-workers from MSKCC have published papers on this since at least 2000 [1], thus making MSKCC a natural place to visit.

The trip

My contact at the MSKCC, Margie Hunt, arranged a number of meetings with people with expertise within subjects related to our project, and I had the opportunity to have informal discussions with

experts in the area of for example hypoxia which is essential in the project. A detailed program for my visit can be found later in this report. Furthermore I had the opportunity to follow some other interesting projects related to radiotherapy in general also contributing positive to my everyday life as a medical physicist. I owe Margie great thanks for a very well organized visit.

My stay in New York gave me several invaluable experiences related to my work as well to visiting the famous city. Besides this I have established contacts to a number of people doing research in groups which are well established internationally. These people have expertise in both radiotherapy in general and in subjects related more directly to the project which I have described briefly above.

At the MSKCC there is a very large nuclear medicine department, which is famous for its research in for example hypoxia. I talked to several people – John Humm, Sadek Nehmeh and Pat Zanzonico just to mention a few. The first two are both authors of a paper on modelling of chronic and acute hypoxia [4]. The results from this paper might be interesting for us in the future when their methods have been refined further to decrease the uncertainties in the predictions of their models.

Most of the people I met were physicists but I also met a radiation oncologist named Nancy Lee. She is working with head and neck cancer and has a number of publications on the impact of hypoxia on the outcome of treatment. [5] is particularly interesting for us because it is shown, through Monte Carlo calculations, that boosting hypoxic regions³ with IMRT improves the tumour control probability. This reminds us of another aspect of the project, namely the need for reliable biological models of the outcome from the treatment of hypoxic cells with carbon ions. Nancy Lee is certainly a capacity who is capable of giving us advice when we need to discuss the project in the future – definitely a good contact!

The last meeting I will mention here is the meeting with Perry Zhang, Assistant Attending Physicist who works with RapidArc development and planning. In our clinic where it is the strategy to use RapidArc to treat many of our patients it was very interesting to talk to a person who is very close to what is going on in the area of research and development. I also got an understanding (or perhaps my thoughts were confirmed) for the complexity and difficulties you are facing when you want to create very complicated dose distributions using RapidArc.

³ The hypoxic regions of the tumour are imaged by Fluorine-18-labeled Fluoromisonidazole positron emission.

Program

Agenda Lars Nyvang February 8-February 12, 2010

Monday, February 8, 2010

- 10:00-11:00 AM: Welcome and tour of Radiation Oncology and Medical Physics:
Margie Hunt, M.S., Associate Attending Physicist, Treatment Planning
Room: R-132
- 11:00-12:00 PM:
Michael Lovelock, Ph.D. Associate Attending, Clinical Physics Service
IGRT
Room: S1119
- 12:00- 1:00 PM: Lunch
- 1:00- 2:00 PM:
Ellen Yorke, Ph.D., Attending Physicist, Treatment Planning
Respiratory Motion Management, Complication Modeling
Room: R-134
- 2:00-3:00 PM:
Nancy Lee, M.D., Associate Attending Radiation Oncologist
Head and Neck Service
Room: SM-15

Tuesday, February 9, 2010

- 9:30-11:30 AM:
John Humm, Ph.D., Attending Physicist, Nuclear Medicine Imaging and
Quantitation
Hypoxia Imaging
Room: Schwartz, 11th floor, Medical Physics
- 11:30-1:00 PM: Lunch
- 1:00-3:00 PM:
Jim Mechalakos, Ph.D., Associate Attending Physicist, Treatment Planning
Treatment Planning, Dose Painting Room: R-130
- 3:00-4:30:
Rachel Bartlett, Ph.D., Sloan-Kettering Institute
Hypoxia Imaging
Room: S 1119

Wednesday, February 10, 2010

- 10:30-11:30:
Sadek Nehmeh, Assistant Attending Physicist, Nuclear Medicine Imaging and
Quantitation
Hypoxia Imaging
Room: 11th floor, Schwartz Building, Medical Physics
- 11:30-1 pm: Lunch
- 1 pm-3 pm:
Treatment Planning Section

Sandra Fontenla, M.S.
General Treatment Planning
Room: R125-D
3:00 -4:30 PM:
Radiation Oncology Grand Rounds
Hoffman Auditorium

Thursday, February 11, 2010

Jitney to Chrysler Building
Jitney departs from MSKCC 1st Ave exit

10:00-11:30 PM:
Perry Zhang, Ph.D., Assistant Attending Physicist, Computer Service
VMAT development and planning
Chrysler Building (646-888-5616)
Check in at Security Desk
12:00-1:30 PM: Lunch
1:30-4:00 PM:
Radiation Oncology Treatment Floor Observation
4th Floor, Radiation Oncology
Please come to M. Hunt's office and she will escort you to 4th floor

Friday, February 12, 2010

10:00-11:00 AM: Wrap- Up
Margie Hunt
Room: R-132
11:00-12:00 PM:
Josh Yamada, M.D., Associate Attending Radiation Oncologist
IGRT Service
Room: S M18

Conclusion

I am very happy to have had the opportunity to visit a famous place like MSKCC with skilled and friendly people. I am sure that I will use at least some of the contacts I created over there, and I definitely got inspiration in many aspects. Last but not least I was glad to be able to present some of our thoughts on a very exotic subject to people who are always very interested in hearing about new and pioneering work.

References

- [1] Clifton Ling et al, Towards multidimensional radiotherapy (MD-CRT): Biological imaging and biological conformality, *Int. J. Radiation Oncology Biol. Phys.*, Vol. 47, No. 3, pp. 551-560 (2000)
- [2] David M. Brizel et al, Oxygenation of head and neck cancer: changes during radiotherapy and impact on treatment outcome, *Radiotherapy and Oncology* 53 (1999) 113-117.
- [3] M. Krämer, Swift ions in radiotherapy – Treatment planning with TRiP98, *Nuclear Instruments and Methods in Physics Research B* 267 (2009) 989-992.

[4] K. Wang et al, Modelling acute and chronic hypoxia using serial images of ¹⁸F-FMISO PET, *Med Phys.* 2009 Oct;36(10):4400-8.

[5] Nancy Y. Lee et al, Fluorine-18-labeled Fluoromisonidazole Positron Emission and Computed Tomography-Guided Intensity-Modulated Radiotherapy for Head and Neck Cancer: A Feasibility Study, *Int. J. Radiation Oncology Biol. Phys.*, Vol. 70, No. 1, pp. 2-13 (2008).