



PanCare Childhood and Adolescent Cancer  
Survivor Care and Follow-up Studies

# PanCareSurFup

May 2014

## PanCareSurFup Bulletin, Issue nr. 7

### PanCare Childhood and Adolescent Cancer Survivor Care and Follow-Up Studies

Dear Friends,

Since Bulletin #6 we have continued the dialogue with the Commission on our Financial report, and the last outstanding issues should be resolved in the near future.

The General Assembly took place in Wroclaw, Poland, on 14-15 May following the 13th PanCare meeting 12-14 May. Lively discussions on both the past and the future work in the project took place within the Consortium. We also managed to have a telephone meeting with our two Scientific Officers, Dr. Dominika Trzaska and Dr. Grzegorz Owsianik where we got good and very relevant information on several important issues for the future.

In this issue of the Bulletin you will learn more about the work in WP2 by the work package leader, Prof. Florent de Vathaire from Institut Gustave Roussy in Villejuif, France. I hope you will learn more about the interesting but difficult topic that is Radiation dosimetry.

I wish you all a long and relaxing Summer!

All the best,

Lars Hjorth  
Coordinator PanCareSurFup

PS. Congratulations to ENCCA who have just been granted a one-year no-cost extension!



Bernarda Kazanowska and co-organiser Maryna Krawczuk-Rybak from Bialystok



Monica Terenziani and Marco Spinelli

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## Latest developments in PanCareSurFup

### Work Package 3

WP3 is the cardiac work package. This work package will study the incidence and risk factors of five different cardiac events (heart failure, ischemia, pericarditis, valvular disease and arrhythmia).

We currently have the cardiac cases in the WP1 database for France, Italy (population based cohort), Slovenia and Switzerland. Hungary, the Netherlands and the United Kingdom will deliver their cardiac cases within the next 3 months. We are on the verge of selecting controls.

To adequately analyse the data from the different countries the CEs need to be graded and validated in a uniform manner across Europe. The validation method used in PCSF WP3 was therefore tested on consistency and validity. The small study showed that the method is very valid and consistent.

Almost all data providers started data collection of chemotherapy and radiotherapy for the cardiac cases and as soon as the controls are selected we can start with the data collection for them.

Preparations for the cohort and case-control analyses also started. We are writing syntaxes for the statistical analyses. A document is written with all the risk factor definitions and evidence behind the risk factors.

### Work Package 5

An important milestone was achieved by Work Package 5 the same week as our PanCareSurFup meeting was held in Wroclaw. The data on "late mortality" cohort were successfully imported from Mainz to Lund. The cohort is still not complete because some providers could not deliver their data yet. Nevertheless this step enables the team in Lund to get acquainted with the present data, to check once more their plausibility and validity, and to start setting up a frame for the statistical analyses. At the same time it opens for a dialogue between Lund and the individual providers regarding details of their data. We are looking forward to this new phase of our work with great enthusiasm and expectations.

### Work Package 6

Current activity within PCSF WP6 has two main strands. Much guideline development work continues. The WP6 Transition Topic subgroup has held four webconferences so far in 2014 and has collected much evidence concerning the definition of transition and descriptions of models of care for transition. Further webconferences are planned and a face-to-face meeting is being arranged to develop guideline recommendations based on this evidence and to plan the final two aspects of evidence collection (implementation strategies and their effectiveness). There are four active joint WP6 / International Harmonisation Group subgroups. The Female and Male Gonadotoxicity groups are both finalising their guideline recommendations and preparing manuscripts for publication, whilst the Thyroid Secondary Cancer subgroup is developing its literature search strategy and the CNS Secondary Malignancy subgroup is recruiting members.



Audience at the 13th PanCare meeting in Wroclaw (12-14 May, 2014)



Tomas Kepak from Brno shows news from the PanCare website



Bernarda Kazanowska, local organizer of both the PanCare and the PanCareSurFup meetings in Wroclaw



In addition, during 2014 there have been several webconferences and meetings of the recently formed subgroups aimed at supporting WP6's overall programme of work. The WP6 Methodology subgroup has held two very productive webconferences to develop a strategy for developing evidence-based guidelines for the many smaller and relatively evidence-poor miscellaneous topics, and it is hoped that guideline development work on these will start in the second half of 2014. The joint WP6/7 Implementation and Feasibility subgroup has held three webconferences to agree its membership and remit and is about to collect information about potential barriers to guideline implementation. The joint WP6/7 PLAIN Information subgroup has held three webconferences and one face-to-face meeting, and has already commenced detailed work looking at how guideline recommendations can be made more understandable for and accessible to survivors and their families.



PanCare attendees on the way to the meeting dinner

## PanCareSurFup Partners

The project's dissemination team interviews Dr Florent de Vathaire from Gustave Roussy, Paris, France, leader of Work Package 2 on radiation dosimetry.

### Can you describe how you got involved in PanCareSurFup?

Gustave Roussy is involved in PanCareSurFup as a major data provider in the case-control aiming to investigate the risk factors of second cancers (WP3) and cardiac diseases (WP4) following childhood cancer. Gustave Roussy is also in charge of the Work Package 2 "Dosimetric reconstruction". The aim of the WP2 is to reconstruct the radiation therapy received by cases and controls of WP3 and WP4 during the treatment of their childhood cancer, and to estimate the radiation doses received to the heart in WP3 and to the site of the second primary cancers in WP4.

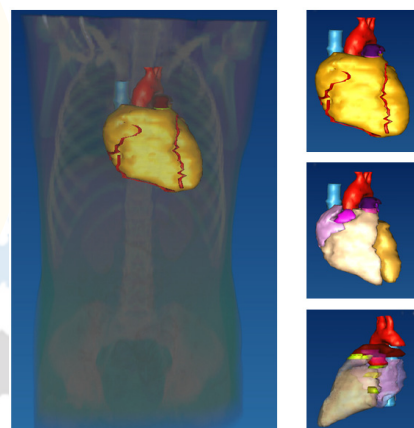
### Could you please define 'radiation dosimetry' and 'radiation therapy reconstruction' in lay language?

'Radiation dosimetry' consists in quantifying the radiation exposure to an individual or to a specific location in its body.

'Radiation therapy reconstruction' is a process aiming to reproduce as accurately as possible the treatment plan of a former radiation therapy patient. Our team is using dedicated software which is working in 3 main steps:

- To model the patient's anatomy in treatment position mainly from its age at the start of the treatment and information in the treatment records.
- To set up the radiotherapy treatment plan by positioning the irradiation fields as closely as possible to the actual treatment, using the treatment records and a large library of radiotherapy treatment units.
- To compute dose calculation to estimate the dose absorbed by the anatomical structures of interest.

This software is constantly improved by our team to increase the accuracy of the radiation therapy reconstruction.

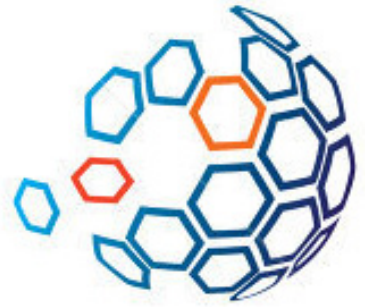


The heart structure as it is in the software that will be used by the PanCareSurFup WP2 for the cardiac case-control study

### Why is your Work Package so important to other WPs in PanCareSurFup?

WP2 is critical in PanCareSurFup because it is the only WP estimating the dose from radiation therapy which is known to be one of the major causes of long term iatrogenic events such as cardiovascular diseases (WP3) or second malignant neoplasms (WP4). Accurate dose estimation to these structures is needed to study the relationship between the radiation dose received to an organ of the body and the risk of latter development of iatrogenic events at this organ.

Dose reconstruction is a time consuming process which as to be performed for each patient of the WP3 and WP4, and needs in average about two hours per patient.



### Can you describe which are the main effects of radiation therapy are on the human body, especially in a growing individual? Why children and adolescents should not receive such radiations?

Radiation therapy is a very efficient and personalised treatment of cancer which aims to deliver high radiation doses to the cancers, while limiting at the minimum the irradiation of healthy tissues which are near to the cancer. Despite regular improvement in radiation therapy technics, these healthy tissues are nevertheless irradiated. For several reasons, which are probably not all identified, children are much more at risk of iatrogenic effects due to the irradiation of healthy tissues than adults. This is true whatever the type of iatrogenic events considered: second cancers, cardiovascular diseases, diabetes, cataracts... Therefore, efforts should be maintained to continue to reduce the irradiation of healthy tissues during childhood cancer radiotherapy.

### What is Work Package 2 aiming to achieve?

WP2 aims to:

- Perform radiation therapy reconstruction and whole body dosimetry for the former patients included in WP3 and WP4 who received radiotherapy.
- Estimate radiation dose received to the heart during radiotherapy, as well as uncertainties in this estimate for WP3 patients.
- Estimate radiation dose received to the specific site of the second malignant neoplasm during radiotherapy, as well as uncertainties in this estimate for WP4 patients.
- To produce a table of standardized dose estimation for organs at risk, for the main types of childhood cancer, for W3 and W4 subjects for whom technical radiation therapy records are lost or unavailable, as well as uncertainties around these estimates.

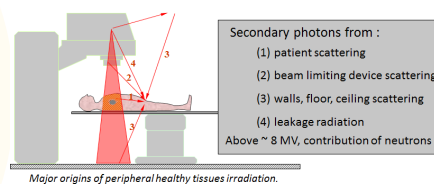
### What are/will be the challenges in achieving its deliverables?

Because of the unexpected long delay in collecting technical records of WP3 and WP4, the main challenge for our group will be to achieve thousands of dose-reconstructions in a very short time frame.

### Is it difficult to find all the necessary data on radiation exposure for each case and control?

Most of the second cancers and cardiac diseases developed after childhood cancer treatment occurred several decades after radiation therapy. Therefore, most of the patients included in WP3 and WP4 were treated a very long time ago, up to the early 1960's, and, in some institutions, it can be very difficult to find now their treatment records.

Figure 1 : Peripheral doses in Radiation Therapy (RT)



Peripheral doses in Radiation Therapy (RT)

**Do you think that the table of standardised dose estimation for organs at risk will be used by healthcare professionals when planning the least harmful form of treatment for a paediatric cancer patient in the future?**

The knowledge of the dose-response for radiation, which will be established in WP3 and WP4, and of the factors modifying this dose response (age, gender, chemotherapy drugs, hormonotherapy, dose-fractionation, etc), rather than the table of standardised dose estimation for organs at risk, will be helpful for anticipating the effects of new radiation therapy technics, and thus for planning less harmful treatments. The table of standardised dose estimation for organs at risk will concern treatments of the past, not of the future. This table will permit clinicians in charge of the medical follow-up of childhood cancer survivors treated in the past to have an idea of the radiation doses received to the most important organs by these survivors during their former treatment. This knowledge is a key factor in order to anticipate the iatrogenic risks to which childhood cancer survivors are exposed.

**Please describe one of your proudest moments or an achievement you are particularly proud of.**

The elaboration of our new dosimetric software needed competences accumulated during a long time in a large range of areas: imaging, physics, analytical mathematics, statistics, computer science and radiation therapy. My group is particularly proud of having achieved this challenge.

**For more information, please contact:**

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This publication has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013), project call HEALTH.2010.2.4.1-7, Predicting long-term side effects to cancer therapy, grant agreement n° 257505.