PROJECT DELIVERABLE

Project acronym: **REQUITE**	GA number: **601826**
Project title: **Validating predictive models and biomarkers of radiotherapy toxicity to reduce side-effects and improve quality-of-life in cancer survivors**	
Funding Scheme: **Collaborative Project (FP7-HEALTH-2013-INNOVATION-1)**	
Project start date: **01 October 2013**	Duration: **60 months**
Project's coordinator: **Prof Catharine West (University of Manchester, UK)**	

Deliverable no.: **D7.2**	Title: **Report on scientific publications, conference presentations and dissemination placed on REQUITE website**
Due date: **Month 60 (30 September 2018)**	Actual date: **Month 62 (27 November 2018)**
Aim of the Deliverable: To provide a final update on the outputs and dissemination activities of the REQUITE consortium to be placed on the REQUITE website. **Deliverable D7.2 has been achieved in full**.	
Lead beneficiary for this deliverable: **Dirk De Ruysscher (B13)**	
Personnel involved: **Catharine West, Rebecca Elliott, Holly Summersgill (B1); Jenny Chang-Claude, Petra Seibold (B2), Liv Veldeman (B3); Chris Talbot, Adam Webb (B4); Tiziana Rancati (B8); Ana Vega, Sara Gutierrez Enriquez (B9); Ananya Choudhury (B10); Barry Rosenstein (B12); Sylvie Canisius (B13); Frederick Wenz (B14); David Azria (B15).**	

Dissemination level:		
PU	Public	**X**
PP	Restricted to other programme participants (within the Commission)	
RE	Restricted to a group defined by the consortium (including the Commission)	
CO	Confidential, only for members of the consortium (including the Commission)	

REQUITE Animation

REQUITE worked with the Dutch company 'Animating Science' (http://animatingscience.com) to make a short animation. In clear, easy to understand language (with audio and text translated into multiple European languages), the animation addresses the concerns and questions of patients who have recently been diagnosed with cancer and expect to receive radiotherapy. It highlights our progress and explains how the work will support future research to help more patients survive and improve their quality of life.

Figure 1: Stills from the patient focussed REQUITE animation

Thanks to treatments such as radiotherapy, more patients are surviving their cancer and thus living longer.
That is great news for patients like Ellen and John.
But we don't know if side effects will have an impact on their quality of life.
Side effects happen when the radiation that kills the cancer also damages healthy tissue.
And a minority of people experience more long term side effects than others.
At the moment we cannot identify how sensitive to radiation Ellen or John may be or if they will suffer long term side effects.
So we need a way to predict radiation sensitivity, so we can improve treatments for each patient.
That is why we founded the REQUITE project.
To find biomarkers that predict radiation sensitivity and improve predictive models.
To, ultimately, reduce long term side effects and improve quality of life for patients.
And one of the important keys we believe, is to be found in genetics.
Ellen and John are two of 4400 patients across Europe who participated in this study by completing questionnaires to record any side effects; donating blood; providing anonymous medical data
These data have been brought together so we can look for the genes that are linked to radiation sensitivity, and test predictive models
Soon, we hope to be able to identify those patients who are radiosensitive.
And to share our findings and anonymous data with other researchers and health professionals so we can improve treatments for patients.
Ellen is lucky, for now, it seems she is not prone to lasting side effects.
John suffered minor inconveniences from his radiation treatment.
But thanks to their contribution, we can pursue the development of personalised cancer treatment.
Whereby future patients may not only just survive but also preserve their quality of life.
For more information about our findings go to requite.eu.

Figure 2: Script from the patient focussed REQUITE animation

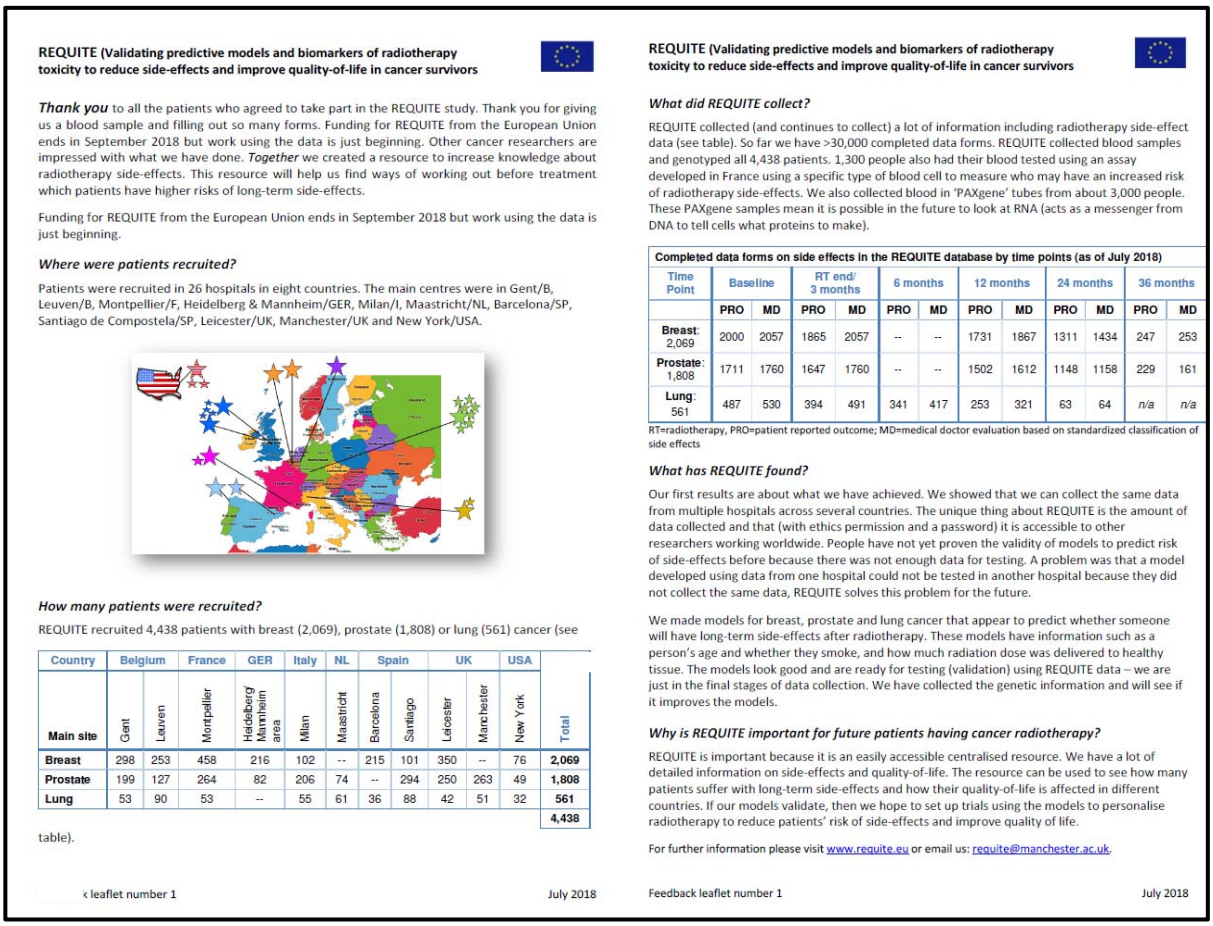
REQUITE Video Shorts

REQUITE also worked with a British company 'Viva La Zoom' (https://www.vivalazoom.co.uk) to film two videos. The patient video is in English but is subtitled in Spanish, French, German, Italian, Dutch and English. Hearing from doctors, scientists and patient advisors who worked on the study it aims to highlight the goals of the international REQUITE study and also thanks every patient who took part because their involvement will help patients in the future who have cancer treatment. A second video (in English) is aimed at doctors and researchers explaining the importance and motivations of the project and promotes the high quality database and biobank that can be made available to support future research.

Figure 3: Stills from the REQUITE patient video (available in multiple languages)

REQUITE Patient Leaflets

An update was written in response to patients asking their local research teams for more information on the progress and results of the study. The leaflet is available in English, Spanish, French, German, Italian and Dutch via the REQUITE website, in paper format from local research teams and was highlighted on Twitter and Facebook.



REQUITE (Validating predictive models and biomarkers of radiotherapy toxicity to reduce side-effects and improve quality-of-life in cancer survivors

Thank you to all the patients who agreed to take part in the REQUITE study. Thank you for giving us a blood sample and filling out so many forms. Funding for REQUITE from the European Union ends in September 2018 but work using the data is just beginning. Other cancer researchers are impressed with what we have done. *Together* we created a resource to increase knowledge about radiotherapy side-effects. This resource will help us find ways of working out before treatment which patients have higher risks of long-term side-effects.

Funding for REQUITE from the European Union ends in September 2018 but work using the data is just beginning.

Where were patients recruited?

Patients were recruited in 26 hospitals in eight countries. The main centres were in Gent/B, Leuven/B, Montpellier/F, Heidelberg & Mannheim/GER, Milan/I, Maastricht/NL, Barcelona/SP, Santiago de Compostela/SP, Leicester/UK, Manchester/UK and New York/USA.

How many patients were recruited?

REQUITE recruited 4,438 patients with breast (2,069), prostate (1,808) or lung (561) cancer (see table).

Country	Belgium		France	GER	Italy	NL	Spain		UK		USA	
Main site	Gent	Leuven	Montpellier	Heidelberg/ Mannheim area	Milan	Maastricht	Barcelona	Santiago	Leicester	Manchester	New York	Total
Breast	298	253	458	216	102	--	215	101	350	--	76	2,069
Prostate	199	127	264	82	206	74	--	294	250	263	49	1,808
Lung	53	90	53	--	55	61	36	88	42	51	32	561
												4,438

k leaflet number 1 July 2018

REQUITE (Validating predictive models and biomarkers of radiotherapy toxicity to reduce side-effects and improve quality-of-life in cancer survivors

What did REQUITE collect?

REQUITE collected (and continues to collect) a lot of information including radiotherapy side-effect data (see table). So far we have >30,000 completed data forms. REQUITE collected blood samples and genotyped all 4,438 patients. 1,300 people also had their blood tested using an assay developed in France using a specific type of blood cell to measure who may have an increased risk of radiotherapy side-effects. We also collected blood in 'PAXgene' tubes from about 3,000 people. These PAXgene samples mean it is possible in the future to look at RNA (acts as a messenger from DNA to tell cells what proteins to make).

Completed data forms on side effects in the REQUITE database by time points (as of July 2018)

Time Point	Baseline		RT end/ 3 months		6 months		12 months		24 months		36 months	
	PRO	MD	PRO	MD	PRO	MD	PRO	MD	PRO	MD	PRO	MD
Breast: 2,069	2000	2057	1865	2057	--	--	1731	1867	1311	1434	247	253
Prostate: 1,808	1711	1760	1647	1760	--	--	1502	1612	1148	1158	229	161
Lung: 561	487	530	394	491	341	417	253	321	63	64	*n/a*	*n/a*

RT=radiotherapy, PRO=patient reported outcome; MD=medical doctor evaluation based on standardized classification of side effects

What has REQUITE found?

Our first results are about what we have achieved. We showed that we can collect the same data from multiple hospitals across several countries. The unique thing about REQUITE is the amount of data collected and that (with ethics permission and a password) it is accessible to other researchers working worldwide. People have not yet proven the validity of models to predict risk of side-effects before because there was not enough data for testing. A problem was that a model developed using data from one hospital could not be tested in another hospital because they did not collect the same data, REQUITE solves this problem for the future.

We made models for breast, prostate and lung cancer that appear to predict whether someone will have long-term side-effects after radiotherapy. These models have information such as a person's age and whether they smoke, and how much radiation dose was delivered to healthy tissue. The models look good and are ready for testing (validation) using REQUITE data – we are just in the final stages of data collection. We have collected the genetic information and will see if it improves the models.

Why is REQUITE important for future patients having cancer radiotherapy?

REQUITE is important because it is an easily accessible centralised resource. We have a lot of detailed information on side-effects and quality-of-life. The resource can be used to see how many patients suffer with long-term side-effects and how their quality-of-life is affected in different countries. If our models validate, then we hope to set up trials using the models to personalise radiotherapy to reduce patients' risk of side-effects and improve quality of life.

For further information please visit www.requite.eu or email us: requite@manchester.ac.uk.

Feedback leaflet number 1 July 2018

Figure 4: REQUITE patient leaflet (available in multiple languages)

Some hospitals also made their own leaflets to thank their patients for joining the study and to explain the importance of their involvement.

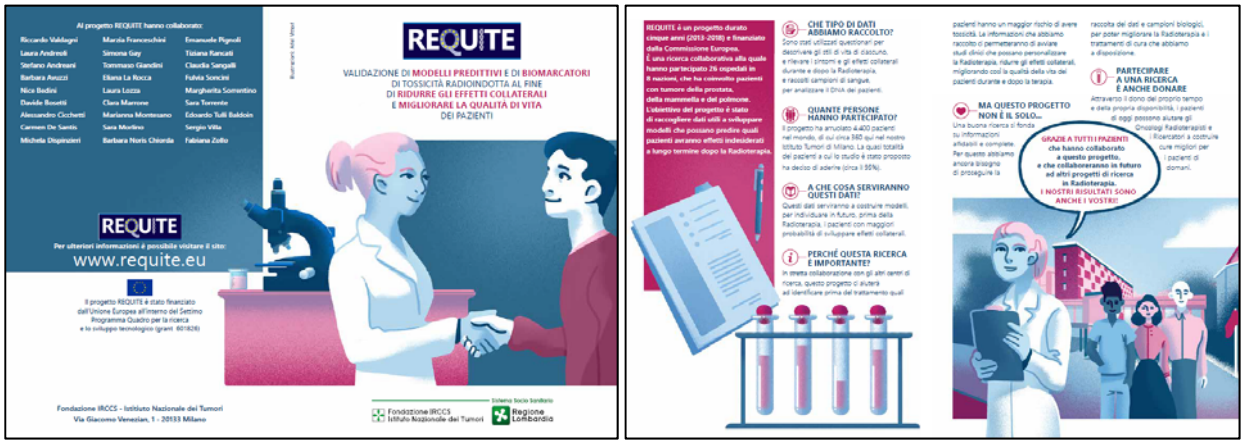


Figure 5: Italian patient leaflet

REQUITE Publications & Presentations

Lists of the REQUITE talks, poster presentations and publications are available from the 'Dissemination' link of the REQUITE website.

Particular highlights include two review articles where members of the Patient Advisory Group helped to write and review the papers, and are therefore named as co-authors:

- Azria David et al. (2017) Data-Based Radiation Oncology: Design of Clinical Trials in the Toxicity Biomarkers Era. Frontiers in Oncology, 7, 83. DOI: 10.3389/fonc.2017.00083
- Ruysscher, Dirk et al (2017) Optimal design and patient selection for interventional trials using radiogenomic biomarkers: A REQUITE and Radiogenomics consortium statement. Radiotherapy and Oncology, 121:3, 440 – 446. DOI: 10.1016/j.radonc.2016.11.003

Also, a paper exploring patient attitudes towards future predictive radiogenomics testing for breast radiation toxicity:

- Rattay, T. et al. (2018) The Patient Perspective on Radiogenomics Testing for Breast Radiation Toxicity. Clinical Oncology, 30:3, 151 - 157. DOI: 10.1016/j.clon.2017.12.001

Training The Next Generation

The REQUITE consortium supported four PhD students in their research. Gilles Defraene (KU Leuven) & Chamberlain Mbah (University of Gent) were funded directly by the EU. Each successfully defended their thesis that made use of REQUITE data, samples and/or resources.

- Gilles Defraene: "Image based quantification of radiation induced lung damage" (KU Leuven, January 2018)
- Chamberlain Mbah: "Challenges in predicting normal tissue toxicity in radiotherapy" (University of Gent, September 2018)
- Tim Rattay: "Predicting acute radiation toxicity in breast cancer"(University of Leicester, February 2018)

- Kerstie Johnson: “Predicting radiotherapy toxicity in patients treated with radical radiotherapy using predictive assays and circadian rhythm” (University of Leicester, July 2018)

Additional undergraduate and postgraduate students also completed research using REQUITE data (two medical students; seven MSc students; four BSc students).

REQUITE Symposium

The final REQUITE meeting took place in Manchester on 18th July 2018. It was open to everyone and explained to patients, doctors, scientists and funders of research about the impact of REQUITE and the availability of the REQUITE resource (database and biobank) for future research.

One REQUITE patient gave a talk sharing her experience of being a cancer patient and explained why she chose to take part in the study. She described how it was important for the patient to be involved in making decisions about their treatment, and that she believes research will help to improve the health-related quality of life of cancer survivors.

REQUITE Resource

Together with the patients, the research teams completed more than 100,000 questionnaires (or case report forms) collecting information on:

- people’s cancer diagnosis
- any treatment they had
- details of side effects they had after treatment
- how they were feeling
- how they rated their quality of life

The database does not contain patient names or identifiable information, the data are anonymous to the researchers. The data are linked to a biobank that stores DNA samples collected from the patients. This is a valuable resource for the international radiotherapy research community to do further research and increase knowledge of the health burden of long-term side-effects in cancer survivors.

REQUITE Data Discovery

To help researchers find out what *type* of data and samples are available, a detailed ‘shop window’ into the REQUITE dataset was created. This Data Discovery Platform has several search options like toxicity, gender or diabetes to allow researchers to find out how many patients have those data or characteristics in the REQUITE database. This platform does not allow access to the data. Access to data and/ or samples is only possible upon request and following careful review by the REQUITE team.