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Report on status of posting results in the study registry(s) for WP3

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Abbreviations

CRF – Case Report Form

CT – Computed Tomography

DICOM - Digital Imaging and Communications in Medicine

DOC - Document

e-CRF – electronic Case Report Form

IRDBB - Image and Radiation Dose BioBank

I-131 – Iodine 131

IUCT – Institut Universitaire du Cancer de Toulouse

MRRE Report Provider 2 – Mainz Radiologie Report Engine 2

NM – Nuclear Medicine

RAI - Radioiodine

RMH – Royal Marsden Hospital

SPECT – Single Photon Emission Computed Tomography

SR - (DICOM) Structured Reporting

UKW – University Hospital Würzburg

UMR – University Hospital of Marburg

WP3 – Work Package 3

1. Introduction

This deliverable describes the upload of results in the study registries for Work Package 3 (WP3) of MEDIRAD. MEDIRAD WP3 is a multicentre prospective cohort that aims to evaluate the impact of low-dose radiation exposure from I-131 radioiodine in thyroid cancer treatment.

The overall objectives of MEDIRAD WP3 are to develop and implement the tools necessary to establish, for the first time in a multicentre setting, the range of absorbed doses delivered to healthy organs in patients undergoing thyroid ablation and the threshold absorbed dose required for thyroid ablation. This could potentially enable patient-specific treatment planning that will minimise the risk to the patient while ensuring a successful outcome.

The activity distribution within the patient as a function of the time was assessed to calculate absorbed dose distributions in the healthy organs (whole-body, lungs, bones, liver, kidneys, spleen, bladder wall, salivary glands and bone marrow), thyroid remnant, and associated lymph nodes. Activity measurements were made with a combination of Single Photon Emission Computed Tomography (SPECT) imaging, whole body retention measurements and blood sampling. As part of WP3, gamma camera imaging and data collection study protocols were developed (Deliverable 3.1) for quantitative imaging of I-131. The quantitative gamma camera imaging schedule is shown in Table 1.

Table 1: Post-RAI patient dosimetry scanning schedule.

Hours post-^{131}I admin.	Mandatory	Optional
6 ± 2 h		WB planar and/or 1-2 bed SPECT(/CT)*
24 ± 4 h	WB planar	1-2 bed SPECT(/CT)*
48 ± 4 h	WB planar and 2-bed SPECT(/CT)*	
72 ± 12 h	WB planar	1-2 bed SPECT(/CT)*
96 ± 12 h	WB planar	1-2 bed SPECT(/CT)*
168 ± 24 h		WB planar and/or 1-2 bed SPECT(/CT)*

* SPECT(/CT) range: base of skull to top of thigh

Patients were included from four centres: Royal Marsden Hospital (RMH) United Kingdom, University Hospital Würzburg (UKW) Germany, University Hospital of Marburg (UMR) Germany and Institut Universitaire du Cancer de Toulouse (IUCT) France.

This document reports the process of uploading data to the two data repositories created to support WP3 / the MEDIRAD project. Image data were uploaded to the Image and Radiation Dose BioBank (IRDBB) (Deliverable 2.3). The IRDBB is a repository for the storage of dosimetry and imaging data. Data stored in the IRDBB, such as image and radiation dose data, can be shared for the use in the clinical research studies involved in the MEDIRAD project. The IRDBB study registry is composed of two main components: a DICOM data repository suitable for managing DICOM data (i.e. mainly radiological images and Radiation Dose Structured Reports) and a Resource Description Framework (RDF) repository (i.e. a database supporting the descriptions of both DICOM and non-DICOM data, and facilitating the requesting of information from the IRDBB repository).

Non-imaging clinical data, initially collected using standardised case report forms (CRFs) in all centres, were transcribed to an electronic CRF (e-CRF). The Mainz report engine (MRRE 2), a web-based reporting platform[1], was employed for the upload of e-CRFs.

Prior to each centre participating in the study, standardised pre-study gamma camera setup and calibration measurements were performed for each camera used in the study. The protocols for these measurements were detailed along the study protocol in Deliverable 3.1. The IRDBB was used to store phantoms for the necessary pre-study calibrations.

2. Data upload to study registry: IRDBB and e-CRF

The MEDIRAD IRDBB study registry consists of KHEOPS (Kheops Inc. 2019), a DICOM study registry, and the MEDIRAD IRDBB for associated non-DICOM data and descriptors which can be queried using the IRDBB user interface (see Figure 1). While the IRDBB was set up to hold the 3D dose distributions and patient-specific dose reports, this functionality was not used due to delays in the dosimetry processing and the closure of the IRDBB at the end of the MEDIRAD project. Nevertheless, upload of 3D dose distributions and reports was implemented and tested in the IRDBB.

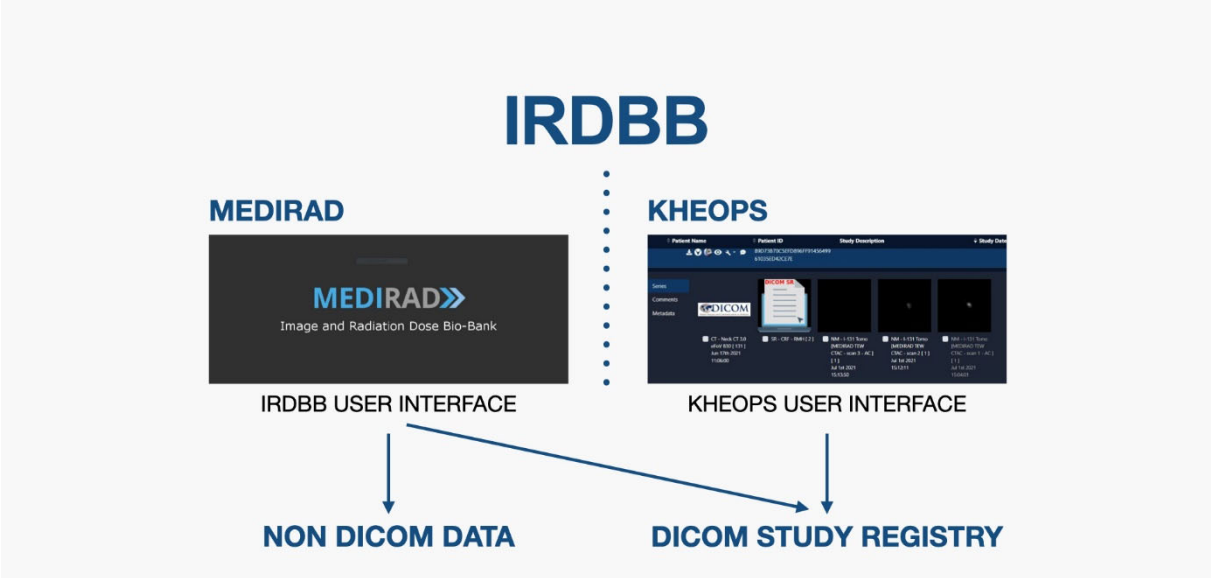

Figure 1. IRDBB Structure.

2.1 Data collected

Data collected during the WP3 clinical studies included DICOM data from different imaging modalities such as Computed Tomography (CT) and Nuclear Medicine (NM), including whole-body (WB) planar images and SPECT images. Furthermore, DICOM structured reports (SR) were used for the e-CRFs. Figure 1 shows an example of imaging and non-imaging data uploaded onto the registry for one of the patients.

Figure 2. Example of data for a patient which includes 3D images of the I-131 distribution scan (SPECT), CT, e-CRF and structured report (SR).

CRFs were developed in conjunction with the clinical teams of WP3. At baseline, the following data was collected in the CRFs:

- Thyroid cancer diagnosis (histology, staging and surgery dates) and patient demographic characteristics.
- Biochemistry results pre-TSH stimulation and post-TSH stimulation which include Thyroglobulin, anti-thyroglobulin, creatinine levels and haematology blood tests.
- Radioiodine treatment details: date, time, reference activity and whole-body measurements;
- Imaging acquired for dosimetry purposes.

Data collected post treatment included routine biochemistry and haematological results as per centre protocol. Reference ranges for the data collected in the CRFs are provided in Table 2.

Table 2: Reference ranges of biochemistry and haematological biomarkers collected as part of WP3.

	RMH		**UKW**		**UMR**		**IUCT**	
	Units	Range	Units	Range	Units	Range	Units	Range
TSH	mU/l	0.465 - 4.68	mU/l	0.3 - 4.0	mU/l	0.34 – 5.6	mU/l	0.38-5.33
FT4	pmol/l	10 - 28.2	pmol/l	11.0 - 23.0	pmol/l	7.5 - 21	pmol/l	7.86-14.4
FT3	pmol/l	4.26 - 8.10	pmol/l	2.7 - 7.6	pmol/l	3.2 – 6.9	pmol/l	3.8-6
Thyroglobulin	ug/l	No reference range	ng/ml	No reference range	ng/ml	3.5 – 77 (with thyroid)	ng/ml	< 1
Anti-thyroglobulin antibody	IU/mL	No reference range	IU/mL	0 - 100	U/ml	-< 40 (old method until 15/10/19) 0 – 4 (new method since 15/10/2019)	U/ml	<4
Creatinine	umol/l	58 - 110 (male) 46 - 92 (female)	mg/dl	0 - 1.17 (male) 0 - 0.95 (female)	mg/dl	0.67 – 1.17 (male) 0.51 – 0.95 (female)	umol/l	59-104 (male) 45-84 (female)
Haemoglobin	g/l	130 – 170 (male) 120 – 150 (female)	g/dl	14 – 18 (male) 12 - 16 (female)	g/l	135 – 172 (male) 120 -154 (female)	g/dl	13-17.5 (male) 11.5-16 (female)
White blood count	x 10^9/l	4.0 - 10.0	x 10^9/l	5 – 10	G/l	3.9 – 10.2	x 10^9/l	4.0-10.0
Neutrophils	x 10^9/l	2.0 - 7.0	x 10^9/l	1.8 - 7.2	%	42 - 77	x 10^9/l	2.0-7.5
Platelets	x 10^9/l	150 - 410	x 10^9/l	150 - 450	G/l	150 - 370	x 10^9/l	150-450

2.2 Storage solutions (IRDBB, KHEOPS and e-CRF)

All anonymised non-imaging data collected in the CRFs were transcribed to the e-CRF using the MRRE2 Provider. For each centre, the principal investigator or an authorized delegate from the study staff was provided access to the e-CRF MRRE2 provider using an authentication based login to the IRDBB. For all centres, an e-CRF template within the MRRE2 was developed to guide transcription of the CRFs (see Figure 2). An example eCRF is shown in Figure 3.

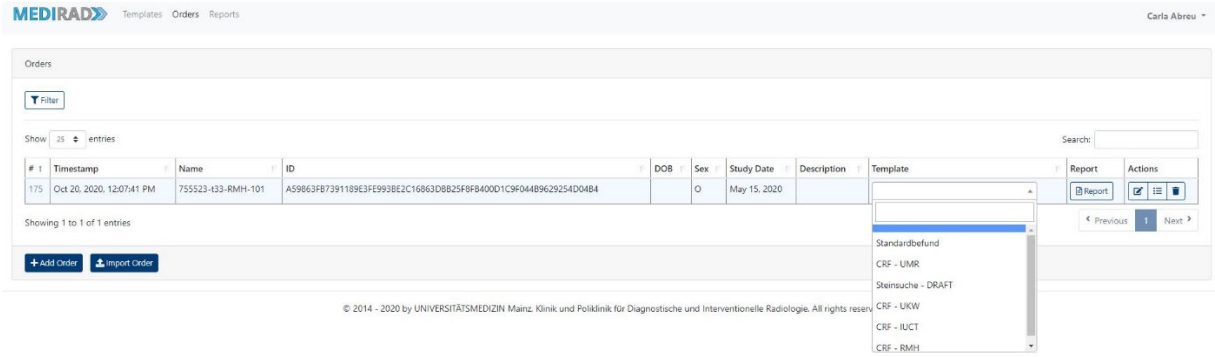

Figure 3. MRRE2 provider interface which allows each centre to select e-CRF template.

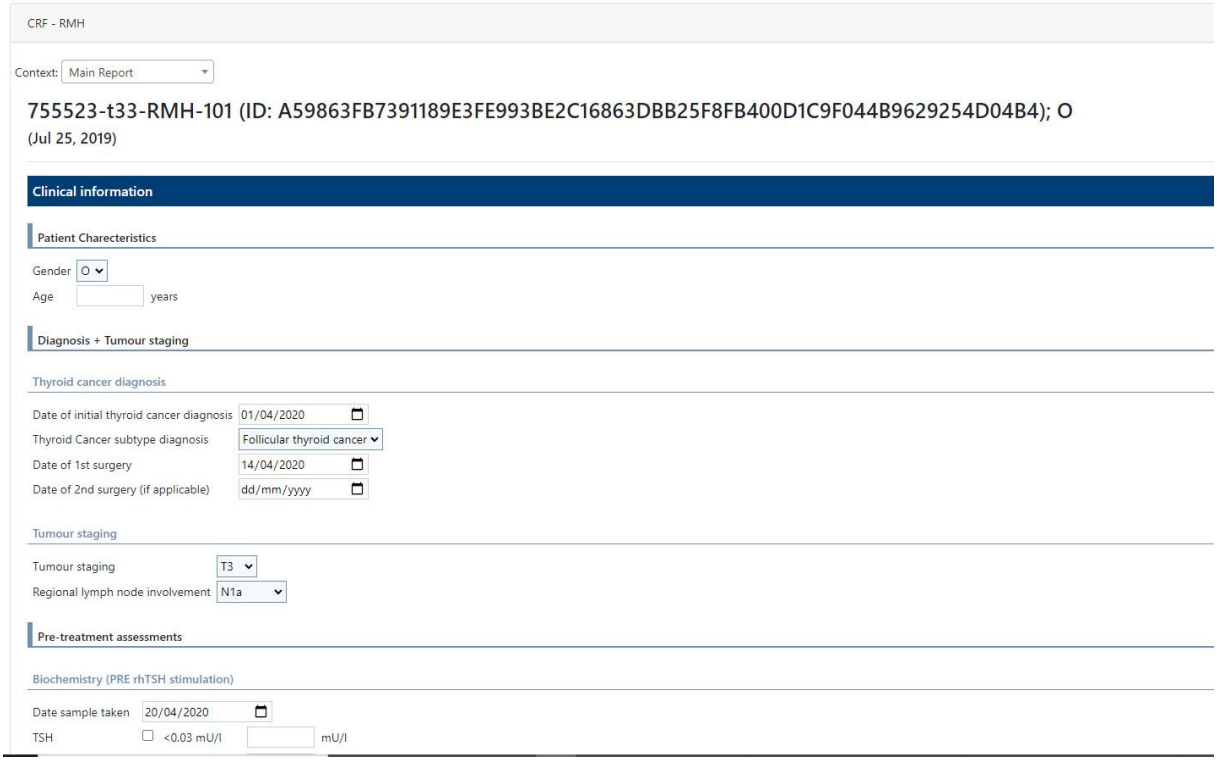

Figure 4. Example of RMH e-CRF data collected for each patient.

Anonymised DICOM imaging data was uploaded to the IRDBB and Kheops. Anonymisation was performed locally at each centre using validated in-house software solutions. The anonymisation processes were tested using phantom data prior to the upload of anonymised patient data. During the upload process, MEDIRAD patient identifiers were assigned following the guidance set out in the "Note to the Data Management Board" provided by WP2. A report about the IRDBB system integration and publication of the basic user guidelines is provided in Deliverable 2.3.

3. Summary of data collected as part of WP3

The description of the patient characteristics presented in the following is based on the data available on the e-CRFs. A total of 106 patients were recruited at the four clinical centres and were uploaded onto the IRDBB platform. The data presented in this report is as of 1 December 2021. All imaging and associated dosimetry non-DICOM data have been uploaded to the study registry. Nevertheless, the follow-up data collection of 22 patients is still ongoing and thus not all follow-up data have been uploaded yet. A single patient eCRF is currently missing, but will be uploaded before MEDIRAD completion. The study population demographic characteristics can be found in Table 3.

Table 3 – Characteristics of the study population

	All n= 106	**RMH n=25**	**Toulouse n=25**	**UKW n=21**	**UMR n= 34***
Age (years, Mean± SD (Range)	47.6 ± 15.5 (18-79)	45.3 ± 15.92 (18-77)	57.3 ± 13.6 (29-79)	42.9 ± 15.0 (19-66)	46.3 ± 11.6 (20-76)
Gender (%)					
Female	84	19	19	17	25
Male	22	6	6	4	9
Cancer Histology (%)					
Follicular	17	9	2	1	4
Papillary	89	16	23	20	30

*34 scans uploaded but one eCRF missing

As per study protocols, different numbers of SPECT and SPECT/CT scans were acquired for patients at the individual centres due to local availability of resources and due to COVID restrictions. A summary of the imaging data collected as part of the clinical studies in WP3 is presented in Table 4.

Table 4 – Number of scans uploaded

	All n= 106	**RMH n=25**	**Toulouse n=25**	**UKW n=21**	**UMR n= 34***
Imaging data acquired		11 single time point patients (1 SPECT/CT per patient) 13 multiple time point patients (2-3 SPECT(/CT) scans)	25 single time point patients (1 SPECT/CT per patient)	21 multiple time point patients with a total of 98 SPECT/(CT) scans (4 to 6 SPECT/(CT) per patient)	34 multiple time point patients with a total of 168 SPECT scans (4 to 6 SPECT per patient)
% of acquired data in repository	100%	100%	100%	100%	100%

*34 scans uploaded but one eCRF missing

Table 5 shows a summary of the number of eCRFs uploaded to the study registry at the time of this report. The number of patients with baseline CRF data and those with complete follow-up data uploaded are presented.

Table 5 – Number of e-CRFS completed

	All n= 106	**RMH n=25**	**Toulouse n=25**	**UKW n=21**	**UMR n= 33**
Baseline	105	25	25	21	33
Follow up	88	17	16	21	33

4. Conclusion

In total, 106 patients from the four different centres have been recruited as part of MEDIRAD WP3. Image data acquired under MEDIRAD were uploaded onto the IRDBB. The focus of this report is on the imaging and dosimetry data available in the study registry, the IRDBB database, as well as on the availability of non-DICOM data such as eCRFs. No further imaging data sets will be uploaded onto the registry.

Of the 105 e-CRFs, 83 have been completed in MRRE2 report 2 and 22 are awaiting follow-up (as per protocol). These are anticipated to be completed by June 2022 and transcription by July 2022. The e-CRFs in the study registry MRRE Report 2 will continue to be updated with the remaining follow-up data once the data has been collected.

5. References

1. Pinto Dos Santos D, Klos G, Kloeckner R, Oberle R, Dueber C, Mildenberger P. Development of an IHE MRRT-compliant open-source web-based reporting platform. *Eur Radiol* 2017; **27**(1): 424-30.