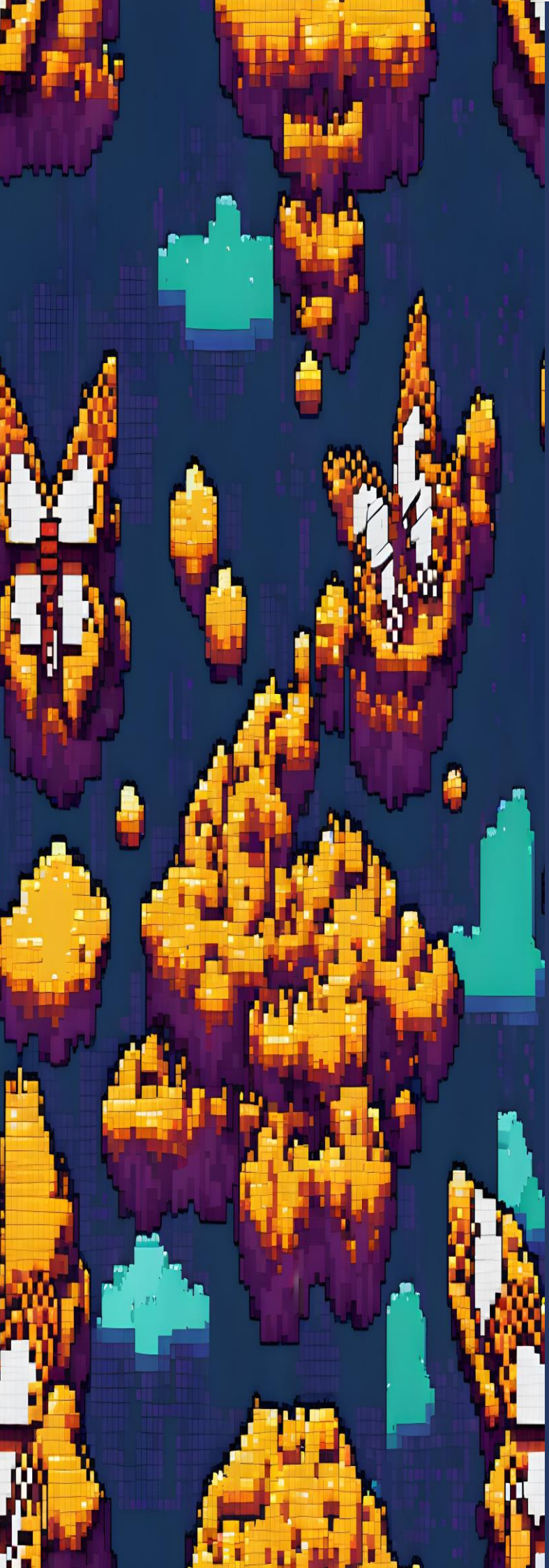

QUANTITATIVE SPECT AND PET IMAGING WITH IODINE NUCLIDES IN THYROID CANCER

F.W.T. Schoffelen

MASTER THESIS TECHNICAL MEDICINE
MEDICAL IMAGING AND INTERVENTIONS

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Abbreviation Glossary

AC	Activity Concentration
AD	Absorbed Dose
BG	Background
COV	Coefficient of Variation
CTAC	Computer Tomography Attenuation Correction
DTC	Differentiated Thyroid Cancer
FDG	Fluorodeoxyglucose
FNA	Fine Needle Aspiration
FOV	Field of View
MTA	Maximum Tolerable Activity
M-TKI	Multi Target - Tyrosine Kinase Inhibitor
NIS	Sodium Iodide Symporter
PET	Positron Emission Tomography
PVE	Partial Volume Effect
RAI-R	Radioactive Iodine - Refractory
RC	Recovery Coefficient
RTK	Receptor Tyrosine Kinase
SPECT	Single Photon Emission Computed Tomography
Tg	Thyroglobulin
TI-RADS	Thyroid Imaging Reporting and Data System
TSH	Thyroid Stimulating Hormone
VOI	Volume of Interest

Preface

In this master thesis I present the research from my graduation internship at the nuclear medicine section of the radiology department in the LUMC. My research is about quantification of radiation in radioactive iodine (RAI) therapy in thyroid cancer patients, with the goal of working towards safe personalized radioactive doses for patients in the clinical practice. In this thesis I first present a general introduction on thyroid cancer and iodine dosimetry, which is followed by Part I about whole body dosimetry with single photon emission tomography (SPECT). Part II is about lesion dosimetry with positron emission tomography (PET). In the following general discussion the potential and future perspectives of dosimetry in thyroid cancer are described. In the final section of my thesis I reflect on my clinical and personal developments in the last year.

Enjoy!

Friso Schoffelen

Quantitative SPECT and PET Imaging with Iodine Nuclides in Thyroid Cancer

Contents

General Introduction

Medical Background

Epidemiology and Etiology

Thyroid cancer has seen an increase in global incidence over the last decades. The incidence tripled in the United States between the early-1980s and mid-2010s and even increased with a factor of 15 between 1993 and 2011 in South Korea, after a national cancer screening campaign.[1,2] It is suggested this rise in global incidence is mostly a result of increased screening with modern imaging modalities, such as ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI), which has led to concerns of overdiagnosis and overtreatment.[1–3] Thyroid cancer mortality has stabilized in high income countries in the same time incidence increased, attesting to the generally excellent prognosis.[4] With 586,202 new cases worldwide in 2020 it comprised 3.0% of all new cancer cases and led to 43,646 deaths.[3] The etiology and underlying molecular mechanisms are still poorly understood. In the past, iodine deficiency was prevalent in low income countries and was known to be the cause of high incidence in benign and malignant thyroid diseases compared to high income countries.[4] Furthermore, neck exposure to ionizing radiation, especially in childhood, is considered a major risk factor.[1,3] However, other etiologic factors have become a focus for new studies recently, such as obesity and environmental pollutants.[1,5]

Thyroid Cancer

The thyroid gland parenchyma is mainly characterized by two cell types. Follicular cells line the colloid follicles and transport iodide inside, where production of thyroid hormones from thyroglobulin (Tg) and iodide takes place. Second, parafollicular C cells that produce calcitonin are found throughout the thyroid interstitium. An illustration with a macroscopic and histological overview is presented in Figure 1. Thyroid malignancy can originate from both cells. Differentiated thyroid cancer (DTC) accounts for 95% of thyroid malignancies and is follicular cell-derived.[6,7] DTC is divided into 3 subtypes, of which the most common is papillary thyroid carcinoma (80%), followed by follicular thyroid carcinoma (10-15%) and oncocytic carcinoma (3-5%, previously known as Hürthle cell carcinoma).[6,8–11] Parafollicular C cell-derived malignancy is known as medullary thyroid carcinoma (5%).[8] Finally, anaplastic thyroid carcinoma (<1%) is an undifferentiated follicular cell-derived thyroid cancer with a median survival of less than 12 months.[6–8] Medullary and anaplastic thyroid cancer are not amenable for iodide therapy and will not be considered further in this report.

Diagnosis and Management

In cases of symptomatic DTC, patients may present with compressive symptoms that include hoarseness, dysphagia and dyspnea. Most thyroid nodules are asymptomatic and are often only found in routine examinations or as incidental findings, usually with ultrasonography. However, only 5-10% of all detected thyroid nodules are malignant.[6] Thyroid nodules on ultrasonography are classified with the Thyroid Imaging Reporting and Data System (TI-RADS) to determine risk of malignancy and the need for fine-needle aspiration (FNA) biopsy.[12] Large nodules with a high TI-RADS score warrant FNA to cytologically classify malignancy. Surgery is the primary treatment for DTC and consists of lobectomy or complete thyroidectomy with or without central and/or lateral cervical lymph node dissection, depending on cytopathologic diagnosis and thyroid tumor size. Thyroid stimulating hormone (TSH) may stimulate growth in remaining tumor cells. Therefore, suppression with supraphysiological thyroid hormone replacement is recommended post-surgery in most patients.[13]

Radioactive Iodine Therapy

Radioactive iodine-131 (RAI) (I-131) ablation is a post-surgical treatment for DTC and is a crucial therapy in patients with high risk of disease recurrence or spread.[14] The aim of RAI therapy is to ablate thyroid remnants and local or distant metastases, reduce the risk of disease recurrence and facilitate follow-up with serum Tg to determine tumor activity.[15] This is done by delivering sufficient absorbed dose (AD) to thyroid cancer lesions. Within 10 years post-surgery, local recurrence and distant metastases occur in 20% and 10% of cases, respectively.[16] RAI therapy has proven to stabilize metastatic DTC.[7,8,17]

RAI-Refractory Disease

The term RAI-refractory (RAI-R) disease describes the groups of patients who no longer respond to RAI. There is no consensus regarding the definition of RAI-R disease. However, the European thyroid association describes four definitions.[18]

1. *Absence of uptake of RAI on scintigraphy*
2. *Absence of RAI uptake in some but not all lesions*
3. *Progression despite uptake of RAI*
4. *Reaching the maximum activity of RAI of 600mCi (22.2 GBq)*

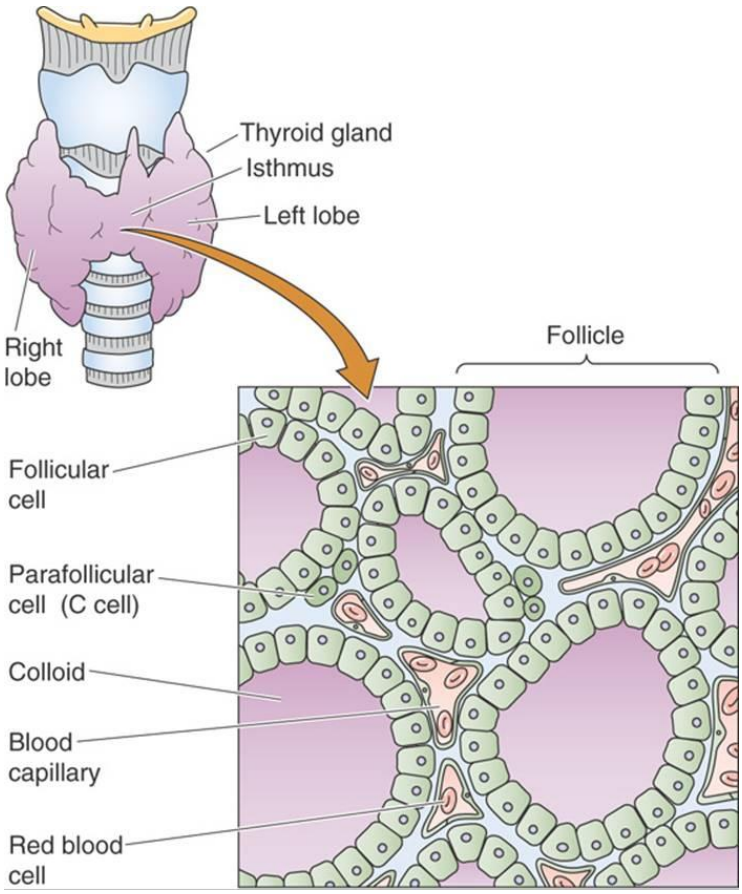

Figure 1. *The macroscopic thyroid and a histological overview of the follicles, follicular cells, C cells, colloid and vascularization of thyroid tissue. Image from:* https://doctorlib.info/physiology/medical-physiology-molecular/50.html

RAI-R thyroid cancer has a poor 10-year survival rate of less than 10% and a median life expectancy of 3-5 years.[19,20]. The ability to accumulate and retain iodide in lesions is lost in 5-15% of DTC patients and in up to 50% of cases with metastatic disease, rendering RAI therapy ineffective.[19] Lack of RAI uptake or retention as well as lack of response despite RAI uptake (radioresistance) are both RAI-R disease, although they differ in mechanism. Especially the mechanisms causing radioresistance are still poorly understood. The standardized management for RAI-R disease is dependent on the number, size, site and rate of growth of lesions and is generally only palliative.[18,21] Local therapy such as surgery or external radiotherapy is recommended in some cases with only few or accessible metastases. For patients with multiple lesions, systemic therapy such as multi-target tyrosinekinase inhibitor (M-TKI) therapy is recommended in case of progression. M-TKI therapy has shown improvement in progression free survival, although not overall survival, in progressive RAI-R patients. However, toxicity was high at effectives doses.[22] M-TKIs that have been approved by the Food and Drug Administration (FDA) and the European Medicines Agency for advanced progressive RAI-R DTC, are lenvatinib, sorafenib and cabozantinib.

Molecular Mechanisms

The process of developing RAI-R disease is associated with the dedifferentiation of thyroid cancer cells. Expression of the sodium iodide symporter (NIS) is essential for RAI uptake.[23] NIS is a membrane protein that facilitates active transport of iodide and is expressed selectively by follicular thyroid cells at their basolateral cell membrane. Its functional expression can be suppressed by aberrancies in receptor tyrosine kinase (RTK) signaling cascades, such as the mitogen-activated protein kinase and phosphatidylinositol-3-kinase pathways that induce cell proliferation and angiogenesis.[19,24] TKIs engage in these pathways, either on multiple targets or only on a single one. A schematic illustration of these mechanism is provided in Figure 2. Ongoing studies are now investigating the use of both single- and M-TKIs in redifferentiating thyroid cancer cells by upregulating NIS expression, thereby reinducing RAI uptake. This would re-enable RAI therapy for refractory patients. Additionally, the toxicity associated with the doses required in first line M-TKI treatment may be avoided.[22,25,26] Studies with single target TKIs in RAI-R patients have shown RAI therapy can be initiated in 40-69% of cases.[24] To determine the efficacy of TKIs as redifferentiation therapy and assess whether patients are eligible for RAI therapy, it is paramount iodide uptake in lesions can be determined prior- and post TKI induced redifferentiation.

Technical Background

Dosimetry

The biokinetics of iodide are highly dynamic and are influenced by lesion characteristics, blood pool composition, renal clearance, TSH levels, thyroid hormone levels and iodine load. Quantification of functional NIS expression, or rather RAI uptake and retention, may play a crucial role in predicting the effectiveness of (reinduced) RAI therapy. The amount of administered I-131 activity (in GBq) should result in a sufficient enough AD (in Gy) in individual thyroid cancer lesions to achieve a favorable therapeutic response. Dosimetry is the determination of the AD in target tissues, which can be achieved by quantitative molecular imaging at multiple time points, using quantitative single photon emission computer tomography (SPECT) or positron emission tomography (PET).

To assess the potential of TKIs as a redifferentiation agent for RAI therapy, pre-therapeutic dosimetry can be used. With prior quantification of RAI uptake and retention in a lesion, therapeutic I-131 activities can be optimized to be as high as achievable without unreasonable radiotoxicity.[27,28] The average dose a target organ absorbs is given by

$$\bar{D}_{r_T}(r_T \leftarrow r_S) = \sum_{r_S} \tilde{A}_{r_S} \times S(r_T \leftarrow r_S), \quad \text{Eq 1)}$$

where $\tilde{A}_{r_S}$ is the cumulated activity in a source organ, r_T the target organ, r_S a source organ and $S(r_T \leftarrow r_S)$ the S-value of a source-target pair.[29] $\tilde{A}_{r_S}$ is given by

$$\tilde{A}_{r_S} = \int_0^\infty A_{r_S}(t)\, dt, \quad \text{Eq 2)}$$

where $A_{rS}(t)$ is the activity in a source organ at time t. The S-value is given by

$$S(r_T \leftarrow r_S) = \frac{1}{M_{r_T}} \sum_i \Delta_i \times \varphi_i(r_T \leftarrow r_S), \quad \text{Eq 3)}$$

where M_{r_T} is the mass of the target organ, Δ_i is the equilibrium absorbed dose constant and φ_i is the fraction of Δ_i that is absorbed by the target organ. Δ_i is given by

$$\Delta_i = E_i \times N_i, \quad \text{Eq 4)}$$

where E_i is the average energy of the i^{th} emission of a nuclide and N_i the yield of that emission per disintegration. Finally, φ_i is determined by the source-target distance, type and volume of the tissues in between and type and energy of the emission. S-values have been calculated this way for many source-target pairs in the body with commonly used nuclides in phantom studies.[30] Generally, the AD in thyroid lesions is caused by self-irradiation. Measuring the iodine uptake in patients over 1-3 assessments can be enough to determine $\tilde{A}_{r_S}$.[31]

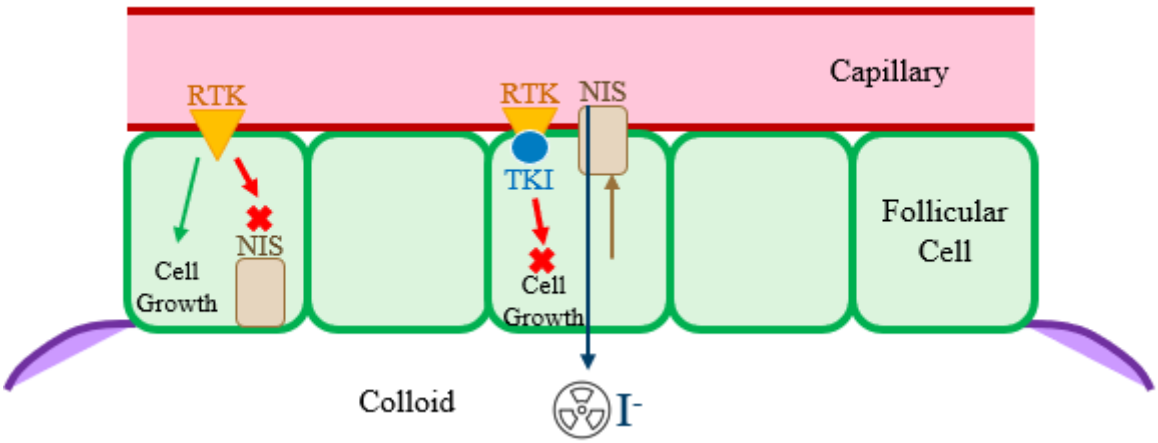

Figure 2. *From left to right: receptor tyrosine kinases (RTKs) activate cell pathways that induce cell growth and inhibit sodium iodide symporter (NIS) expression in follicular thyroid cells. Tyrosine kinase inhibitors (TKIs) engage with targets in these pathways and inhibit them. Re-induced functional NIS expression is a secondary effect of TKIs.*

Simultaneously, the AD in organs at risk, primarily bone marrow and lungs, should not exceed life-threatening toxicity levels. Blood sampling for bone marrow dosimetry and total body iodine retention provide the main determinants of radioactive toxicity.[27,32] Recommended maximum limits are an AD of 2 Gy to the blood and a whole body retention after 48 hours of 2.96 and 4.44 GBq with and without iodine-avid diffuse pulmonary metastases, respectively.[33–35] The maximum tolerable activity (MTA) is defined as the maximum I-131 activity that can be safely administered to a patient without exceeding these limits. Over time, I-131 activity in the body will decrease until it is indistinguishable from background (BG) radiation. The slowest at which this can theoretically happen in the body, is at the rate of the physical decay of I-131, which has a half-life of 8.0 days.

RESET Study

An ongoing single-center study at the Leiden University Medical Center (LUMC) by Dotinga et al., entitled "REinducing radioiodine-SEnsitivty in radioiodine-refractory Thyroid cancer using lenvatinib" (RESET), is currently investigating the use of the M-TKI lenvatinib in redifferentiating RAI-R patients.[36] The main objective of the study is *"to determine the fraction of RAI-R patients who are eligible for I-131 therapy after lenvatinib using I-124."* One of the secondary objectives of the study is *"to assess the agreement between absorbed doses using pretherapeutic I-124 PET/CT dosimetry and intra-therapeutic I-131 SPECT/CT dosimetry."* Calculations of AD in tissue are prone to errors due to the inherent uncertainty of the measuring process in PET/CT and SPECT/CT.[37,38] Therefore, standardized validation and calibration of each individual scanner is paramount to reduce error and allow for comparison of dose calculations in the future and across multiple centers. The goal of redifferentiation studies, such as RESET, is to move towards personalized dosimetry for DTC and RAI-R patients. In turn, the goal of personalized dosimetry is to keep within the personal MTA and give the personal activity needed to deliver the highest dose to lesions. The dose needed to induce a therapeutic effect depends on DTC lesion size and location and can vary between 60-650 Gy.[24,39,40] A dose of ≥100 Gy is commonly accepted to achieve ablation of DTC lesion.[41]A threshold of ≥20 Gy was chosen in the RESET study as a meaningful dose to warrant RAI therapy.[36]

I-131 SPECT/CT

I-131 primarily decays by 606 keV beta minus (89.9%) and 364 keV gamma photon (81%) emission. Its half-life is 8.0 days. The high energy of the beta particles allows them to penetrate tissue up to several millimeters. Within this penetration range they deposit their energy into surrounding molecules, break molecular bonds such as single and double strand DNA and therefore ablate tissue. Gamma photons from decaying I-131 nuclides can be detected with gamma cameras, which allows for imaging of iodide uptake in the whole body and thyroid cancer lesions with planar or SPECT/CT acquisitions, by measuring gamma photon count rate per second (cps). SPECT dosimetry with I-131 has disadvantages. The sensitivity and resolution of current gamma cameras are limited for accurate dose quantification, especially in small lesions. Pretherapeutic administration of I-131 may induce a small unintended therapeutic effect, leading to a decreased response (stunning) during subsequent RAI therapy.[42] Other iodine isotopes that have been investigated include I-123 and I-124. I-123 is a gamma emitter with a half-life of 13.22 hours, which may be too short to determine biokinetics.

I-124 PET/CT

The isotope I-124 emits positrons and can be quantitatively imaged with PET, which offers much better sensitivity and resolution compared to SPECT. A positron annihilation event yields two 511 keV gamma photons that travel in nearly exact opposite direction. The half-life of I-124 is 4.2 days and it has a complex decay scheme. I-124 has a rather large yield of gamma photon emissions,

called prompt gammas, that can fall within the measurement window centered at 511 keV. Especially the 603 keV gamma photon (11.7%) may cause false coincidences with a 511 keV photon. Furthermore, it has a suboptimal positron yield of 23%, which may lead to errors in measurements.[43] Nevertheless, I-124 is currently the most well-suited isotope for pretherapeutic dosimetry. This is because of the favorable half-life and the fact that no stunning has been reported up to 222 MBq.[44] Activity measurements and cumulated activity with I-124 require correction for the difference in half-life when applied in predictive dosimetry calculations for I-131. To harmonize quantitative PET imaging, the European Association of Nuclear Medicine (EANM) has launched an initiative for the optimalization and standardization of acquisition and reconstruction protocols in PET, entitled EARL.[45,46] Centers can acquire EARL accreditation to facilitate quantitative PET. Accreditation is gained by performing quality control experiments and meeting quality requirements described by EARL. However, no EARL program for I-124 exists currently. Instead, the EARL F-18 protocols are used in the RESET study, as the next best option to facilitate harmonization in quantification.

Validation

Given the (dis)advantages of I-131 and I-124, Dotinga et al. developed an iodine dosimetry strategy for the RESET study in the LUMC. This strategy consists of pretherapeutic lesion and toxicity dosimetry with I-124 to predict the AD in lesions and the MTA, as well as intra-therapeutic lesion and toxicity dosimetry with I-131 to validate the predictions and correlate the lesion AD with disease response (with F-18-fluorodeoxyglucose (FDG) PET/CT). Validation of the contemporary SPECT/CT and PET/CT systems are required for this dosimetry strategy. This report investigates two elements of this DTC iodine dosimetry strategy: intra-therapeutic toxicity dosimetry with I-131 SPECT/CT and pretherapeutic lesion dosimetry with I-124 PET/CT.

As illustrated in the flowchart in Figure 3, multiple effects such as scatter, attenuation, collimator, dead-time and partial volume effects affect the accuracy of quantitative SPECT. Improved iterative reconstruction methods incorporating correction for collimator-detector response, scatter, attenuation and resolution recovery, have been developed and investigated.[47] However, we were not able to find a validated correction method for dead-time effects. A detector's sensitivity can be expressed as a function in cps/Bq. Generally, the relation between cps and Bq in a detector is linear. However, losses in counts may occur, due to saturation of the detector.[48] The dead time of a detector is a small time period in which a detector element processes an incident gamma photon and is unsensitive to other gamma photons. A gamma camera can be paralyzable where each new photon detection event resets the dead-time period, or non-paralyzable where the system is insensitive to new events during the dead-time period.[49] It is paramount a dead time correction factor can be applied in quantitative SPECT camera measurements, given 3.7, 5.5 and 7.4 GBq are common therapeutic activities in DTC and given the whole body retention toxicity limits.[24]

For I-124 PET/CT, it is believed the most optimal first step to accurate quantitative measurements is by meeting the EARL requirements as set for F-18-FDG. The standard quality control experiments described by EARL are aimed at quantifying resolution and uniformity. The partial volume effect (PVE) causes losses in counts due to limitations in spatial resolution. For small lesions, the number of voxels that only contain lesion edges account for a larger portion of the total lesion voxels, compared to large lesions. Therefore, activities in small lesions are typically underestimated as a result.[51,52] A recovery coefficient (RC) can be used to correct for PVE. An RC is the ratio between the true and measured activity concentration (AC) for a specific volume.[53,54] RCs for different volumes with the same AC can be plotted in a curve and are used to correct for PVE.

Research Question

A GE Discovery NM/CT 670 Pro SPECT/CT system and GE Omni Legend (32 cm) PET/CT system will be used in the RESET study for I-131- and I-124-dosimetry respectively. These imaging systems both require validation for the respective radionuclides to ensure the most accurate and precise measurements possible. The main research question is:

How can accurate and precise quantification of I-131 and I-124 in lesions and whole body be achieved with contemporary SPECT and PET systems?

The answer to the question above lies in the investigation of the major variables, physical and computational, of SPECT and PET. This report mostly investigates correction for the physical variables in intra-therapeutic I-131 toxicity dosimetry and pretherapeutic I-124 lesion dosimetry. There are two main parts of this report. The first and largest part is on I-131 radiotoxicity dosimetry and the second part is on I-124 lesion dosimetry.

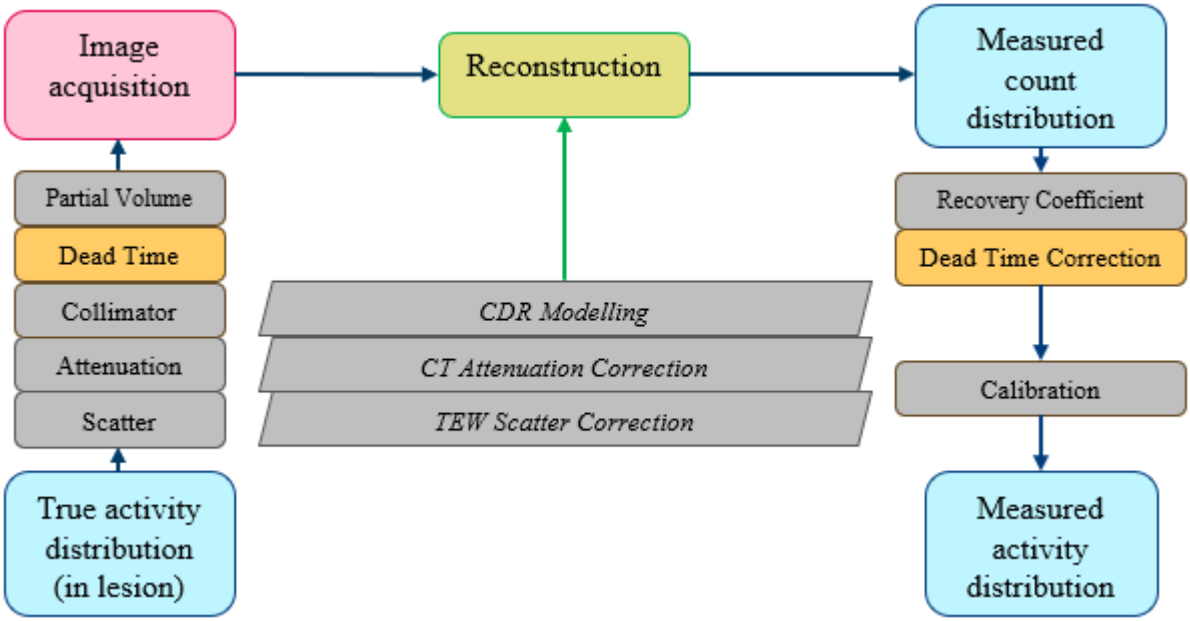

Figure 3. *A flowchart that schematically illustrates the challenges to achieve accurate measurements of an activity distribution. The dead-time effect is highlighted in orange. Image inspired by Westerbergh et al.*[50]

Part I: Radioactive Toxicity Dosimetry with I-131 SPECT/CT

Part I: Aim and Hypothesis

Given the challenges with high early intra-therapeutic activities, the question for Part I is:

Can dead-time effects be characterized and corrected for I-131 intra-therapeutic dosimetry with contemporary SPECT/CT in differentiated thyroid cancer?

The hypothesis for the dead-time characteristics of this SPECT system is that it is a paralyzable system.[53,55,56] It was assumed the behavior of the SPECT gamma cameras are linear with low I-131 activities until a cutoff activity. Figure 4 provides an illustration of the hypothesized characteristics. Part I proposes the following aims:

1.1 Determine detector dead-time characteristics for I-131 activities up to 7.4 GBq

1.2 Determine the SPECT/CT calibration and uniformity characteristics for I-131 activities in the linear range

Part I: Methods

Uniformity

To achieve aim 1.2 a phantom experiment was performed using a homogenous liquid volume of sodium iodide I-131 solution. A 6,726 mL cylindrical uniformity phantom was filled with distilled water and 203 MBq of sodium iodide I-131 was added and distributed uniformly. A validated dose calibrator (VIK-202; Comecer) was used to measure the activity administered to the uniformity phantom and residual activity in syringes or vials. An illustration of the uniformity phantom is presented in Figure 5. The activity was assumed to be low enough to avoid dead time effects. In total 5 SPECT/CT scans were acquired in 2 weeks when the I-131 AC was 30.2, 21.4, 16.6, 9.9 and 5.8 kBq/mL, respectively. The acquisition parameters consisted of high energy general purpose (HEGP) parallel hole collimators, body contouring detector movement, 72 projections (5°/projection), 120 s per projection, a slice thickness of 2.5 mm and an image matrix of 128 × 128. The CT protocol used was clinical standard low dose helical. SPECT/CT image reconstruction was done with ordered subset expectation maximization (OSEM) iterative reconstruction (4 iterations, 10 subsets), triple energy window scatter correction (318 ±3% keV,

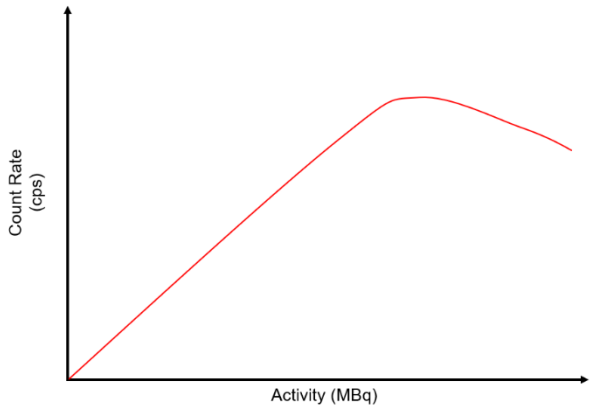

Figure 4. *The hypothesized dead-time behavior of a gamma detector, which is linear as activity increases, until dead-time effects occur and detector performance drops.*

364 ±10% keV and 413 ±3% keV), CT attenuation correction (CTAC) and without post-filtering. Due to human error, no CT was available for the first acquisition. Only the last 4 of the 5 acquisitions were therefore reconstructed. A spherical and cylindrical volume of interest (VOI) with a diameter (and height) of 15 cm, were placed in the center of the phantom in the SPECT scan, using PMOD 4.2 (PMOD Technologies LLC, Fällanden, Switzerland). The mean (±standard deviation (SD)) and max voxel values were calculated from each VOI. Within the linear range of the SPECT system, the calibration factor from cps to activity is

$$C_F = \frac{R_m}{A}, \qquad \text{Eq 5)}$$

where R_m is the measured count rate and A is the activity. The calibration factor C_F was determined with Equation 5, by fitting a line to the means.

Dead-Time Characteristics

A series of phantom studies were performed to determine the gamma camera sensitivity and dead time characteristics for I-131 for a Discovery NM/CT 670 Pro SPECT/CT; GE Healthcare. All remaining experiments described in Part I used 2 detector 'H-mode' planar acquisition, HEGP collimators and a photopeak-energy window of 364 ±10% keV.

To achieve aim 1.1 a point-source phantom experiment was performed. A sodium iodide I-131 capsule was placed anterior in a cylindrical polymethyl methacrylate thyroid scatter phantom to simulate the attenuation and scatter of radiation in the neck. The SPECT gamma cameras were placed in the H position, placing them anterior and posterior to the phantom. The phantom was placed 10 cm below the anterior detector for planar acquisitions. The posterior detector was placed as close as possible to the table. Capsules with activities up to 7.4 GBq were used, to resemble therapeutic RAI quantities. A series of static planar scans were acquired once to twice a week over a period of 3 months. In total, 21 measurements with activities between 85-7,338 MBq were performed. An illustration of this setup is given in Figure 6. Both detectors were used for simultaneous acquisitions, with a 180 s acquisition time and a 256 × 256 image matrix. In total, 4 different capsules were used over this period (2 capsules of 7.4, 1 capsule of 3.7 and 1 capsule of 0.25 GBq). Count rates were extracted from the planar images, by counting from the whole image view, using MATLAB R2022b (Mathworks, Massachusetts, USA). The MATLAB code is provided in the Appendix. In the non-linear range of the detectors, the response for a paralyzable system is described by Sorenson's model,

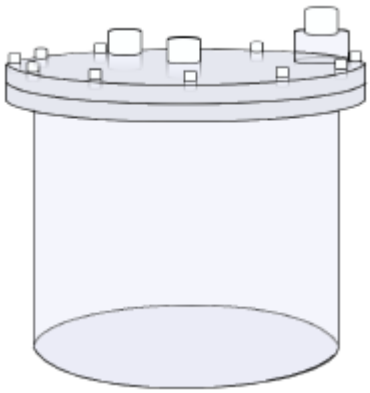

Figure 5. *The Uniformity phantom*
Image from: Westerbergh et al. [50]

$$R_m = R_t \cdot e^{-R_t \cdot \tau}, \quad \text{Eq 6)}$$

where R_m and R_t are the measured and true count rates and τ is a fit parameter (dead-time constant).[57] For dosimetry purposes, this equation was adjusted to use activity instead of the true count rate, giving

$$R_m = \beta \cdot A \cdot e^{-A \cdot \tau}, \quad \text{Eq 7)}$$

where β is another fit parameter. Using MATLAB CurveFitter, lines (Equation 5) were fitted to the lowest 6 measurements, which were assumed to be within the linear range. In CurveFitter, the option to ensure the fitted lines pass through the origin was selected. For the remaining high activity measurements, Sorenson's model (Equation 6) was fitted using the custom function option in CurveFitter. A NonlinearLeastSquares Trust-Region algorithm was used in MATLAB CurveFitter for both types of fits. The intersection point between the line and Sorenson's model (i.e. the cutoff) was then determined in MATLAB for the anterior and posterior detectors. Calibration curves for both detectors were plotted, using the linear fits until the cutoff value and Sorenson's fit after the cutoff value.

Patient Total Body Scan

After performing the dead-time measurements, it was investigated whether this developed model could be used to determine the total I-131 activity in a patient. One clinical DTC patient who received regular RAI therapy (5.7 GBq) was scanned 1,5 hours post-administration on the SPECT system. The patient did not micturate in between administration and scanning, thus we assume no biological loss of activity. The administered activity was corrected the physical decay in between administration and acquisition. Using a step-and-shoot protocol, the patient was scanned in 5 non-overlapping planar spot-views. The same acquisition parameters from the dead-time measurements were used in each spot-view. Using MATLAB, the count rates were determined in

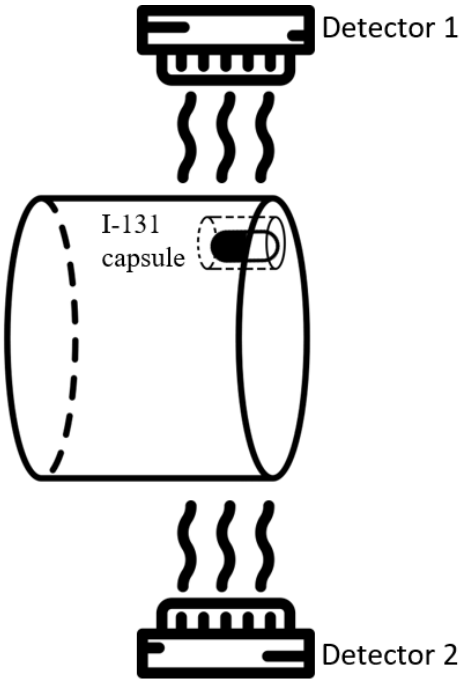

Figure 6. *Schematic illustration of the measurement setup with an anterior and posterior gamma camera (Detector 1 and Detector 2, respectively). In between the detectors a thyroid phantom with I-131 capsule was measured.*

each spot-view for both detectors and corresponding activities were determined with the model. The found activities were summed up and compared to the activity that was present in the patient at the time of acquisition. Two possible activities could technically correspond with the count rate of a spot-view, given the shape of the paralyzable behavior of the gamma cameras, often consisting of a lower and a higher activity. However, for detector 2 the higher possibility suggested the presence of activities greater than 5,7 GBq in a single spot-view, which was assumed not possible. Therefore, the lower possible activity was chosen for the detector 2 spot-view count rates. Of the possible activities given by detector 1, the activity mathematically closest to the activity determined by detector 2 was selected each time. Both were then averaged for each spot-view and summed.

Geometry and Field of View

In a variation of the dead-time experiment, one measurement with a 3.2 GBq I-131 capsule was repeated 5 times, in which the phantom-detector distance was increased for both detectors with increments of 5 cm, up to 35 cm (from the perspective of the anterior detector). Another variation of the experiment was performed three times, each time on a different day, with two I-131 capsules and varying distances between the capsules. One capsule was positioned in the phantom. The second capsule was placed on the table along its axial axis on the caudal edge of the FOV. This measurement was repeated after moving the second capsule with increments of 10 cm, up to the end of the table (2 m) in caudal direction on the table. These experiments are summarized in Table 1. An illustration of this experiment is provided in Figure 7.

Part I: Results

Uniformity I-131

The 4 SPECT/CT measurements of the uniformity phantom are plotted in Figure 8. The linear line fitted to the 4 measurements resulted in a calibration factor of 8.5 voxel value/kBq/mL.

Dead-Time

A total of 21 count rates measured between activity levels of 85 MBq and 7,338 MBq are plotted in Figure 9. The two detectors show a different response to the I-131 capsule in the phantom. Lines were fitted to the 6 lowest measurement (85-662 MBq) for both detectors, as dead-time effects were visually observed for the 7th measurement point for detector 1, which would have resulted in an R^2 of 0.7 for the linear fit. The results of the linear fits were

$$ANT.R_m = 35.22 \cdot A,$$

for the anterior detector (Detector 1) and

$$POS.R_m = 14.66 \cdot A,$$

for the posterior detector (Detector 2), with R_m in kcps and A in GBq. R^2 was 0.9167 and 0.9929, respectively.

TABLE 1

Overview of setups and I-131 capsules used in the FOV experiments

FOV Experiment	I-131 Capsule in phantom (MBq)	2nd I-131 Capsule on Table (MBq)
1	154	634
2	222	640
3	120	344

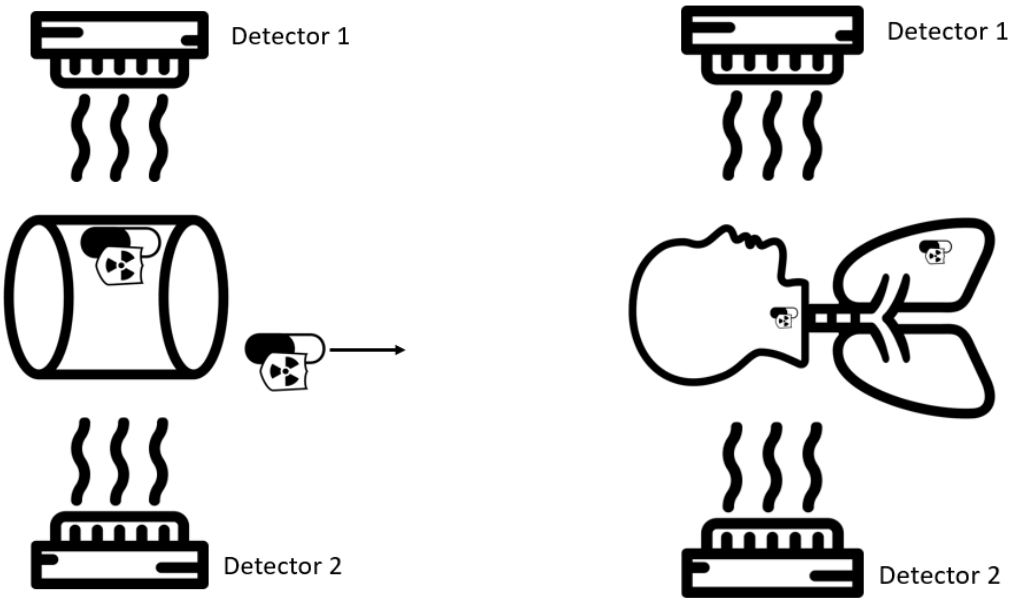

Figure 7. Left. *The experiment setup of the FOV experiments with two I-131 capsules.* **Right**. *The situation the experiment simulates, in which activity, for example in the lungs outside the FOV, may act as a disruptive source for measurements of the thyroid tissue in the neck in the FOV.*

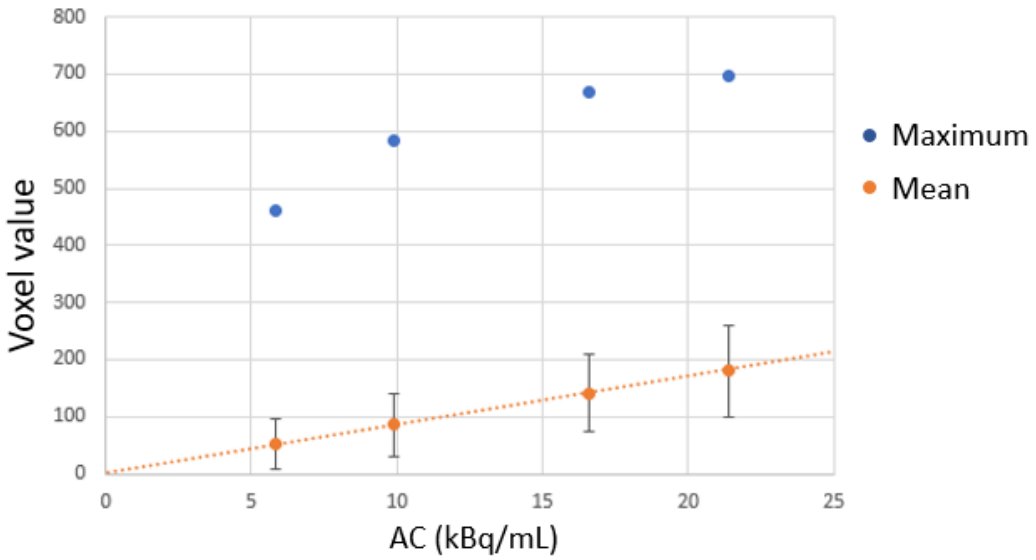

Figure 8. *The results of 4 uniformity phantom measurements with ACs of 21.4, 16.6, 9.9 and 5.8 kBq/mL, respectively. A straight line has been fitted to the 4 measurement points. The y-axis is presented in voxel values, which are the values received directly from PMOD. The standard deviation is shown as an error bar.*

The fit of Sorenson's model to the remaining 15 measurements (1,070-7,338 MBq) yielded

$$ANT.R_m = 66.93 \cdot A \cdot e^{-A \cdot 0.90}$$

and

$$POS.R_m = 18.59 \cdot A \cdot e^{-A \cdot 0.30},$$

for Detector 1 and 2, respectively. Again, R_m is in kcps and A in GBq and R^2 was 0.9963 and 0.9613, respectively. The fits are illustrated in Figure 10. The line and Sorenson's model intersect at 710 and 801 MBq for Detector 1 and 2, respectively, as illustrated in Figure 11. The anterior detector (Detector 1) shows a peak of 27.2 kcps at 1.1 GBq, whilst the posterior detector (Detector 2) shows a peak of 23.0 kcps at 3.4 GBq.

Patient Total Body Scan

The anterior spot-views are illustrated stitched together in Figure 12. The total activity found in the patient was 6.9 GBq, which is an overestimation of 22% compared to the 5.7 GBq present in the patient at the time of acquisition.

Geometry and Field of View

The results from the experiment in which the phantom-detector distance was varied are plotted in Figure 13. At a distance of 15 cm the count rate increased with 1.9 and 0.2 kcps every 5 cm and a total increase of 75.6 and 3.1% at 35 cm was observed for the anterior and posterior detectors, respectively. The results from the first of the three FOV experiments, where the distance of a second I-131 source to the FOV was varied, are plotted in Figure 14. An increase in count rate of 31 and 50% was seen between the FOV edge and at 20 cm, for the anterior and posterior detectors, respectively. Experiment 2 and 3 of the FOV experiments are plotted in Figure 15.

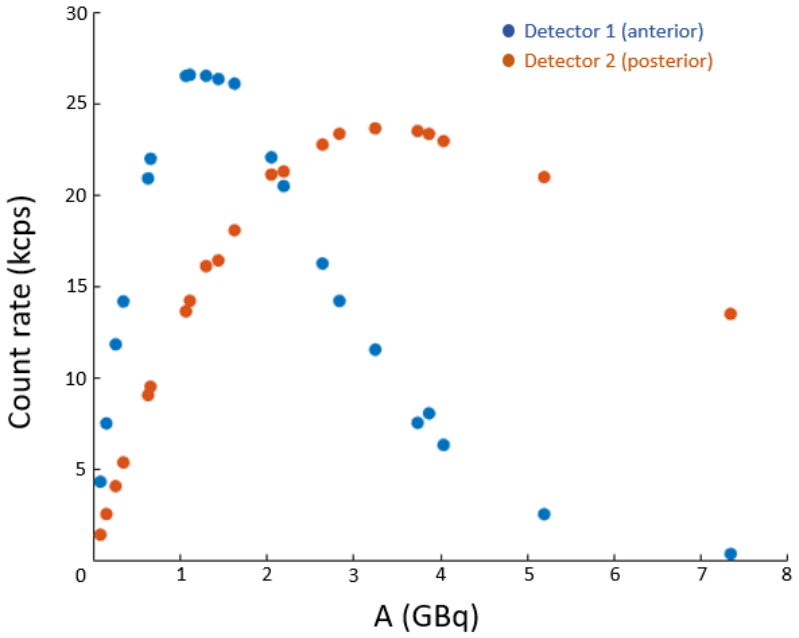

Figure 9. *Scatterplot of count rates at 21 different I-131 activities between 85 MBq and 7.3 GBq.*

In FOV experiment 2 an increase was observed of 160 and 562% in kcps when placing a 640 MBq capsule in the FOV next to the phantom that already contained a 222 MBq capsule. When placing the 640 MBq capsule at the FOV edge an increase of 26 and 33% was observed, respectively. At ≥20 cm the increase in kcps stabilized between 0-3 and 0-5%, respectively. When switching the position of the capsules, the percentages were 16 and 83%, 1 and 4% and 0-1% for both detectors at ≥10 cm, respectively.

In FOV experiment 3, a 120 MBq source in the phantom and a 344 MBq capsule as a second source were used. The percentages were 181 and 704%, 32 and 42%, stabilizing between 2-4% and 5-6% at ≥ 20 cm, respectively. When switching capsules this was 22 and 96%, 3 and 5% and 0-1% for both detectors at ≥10 cm, respectively.

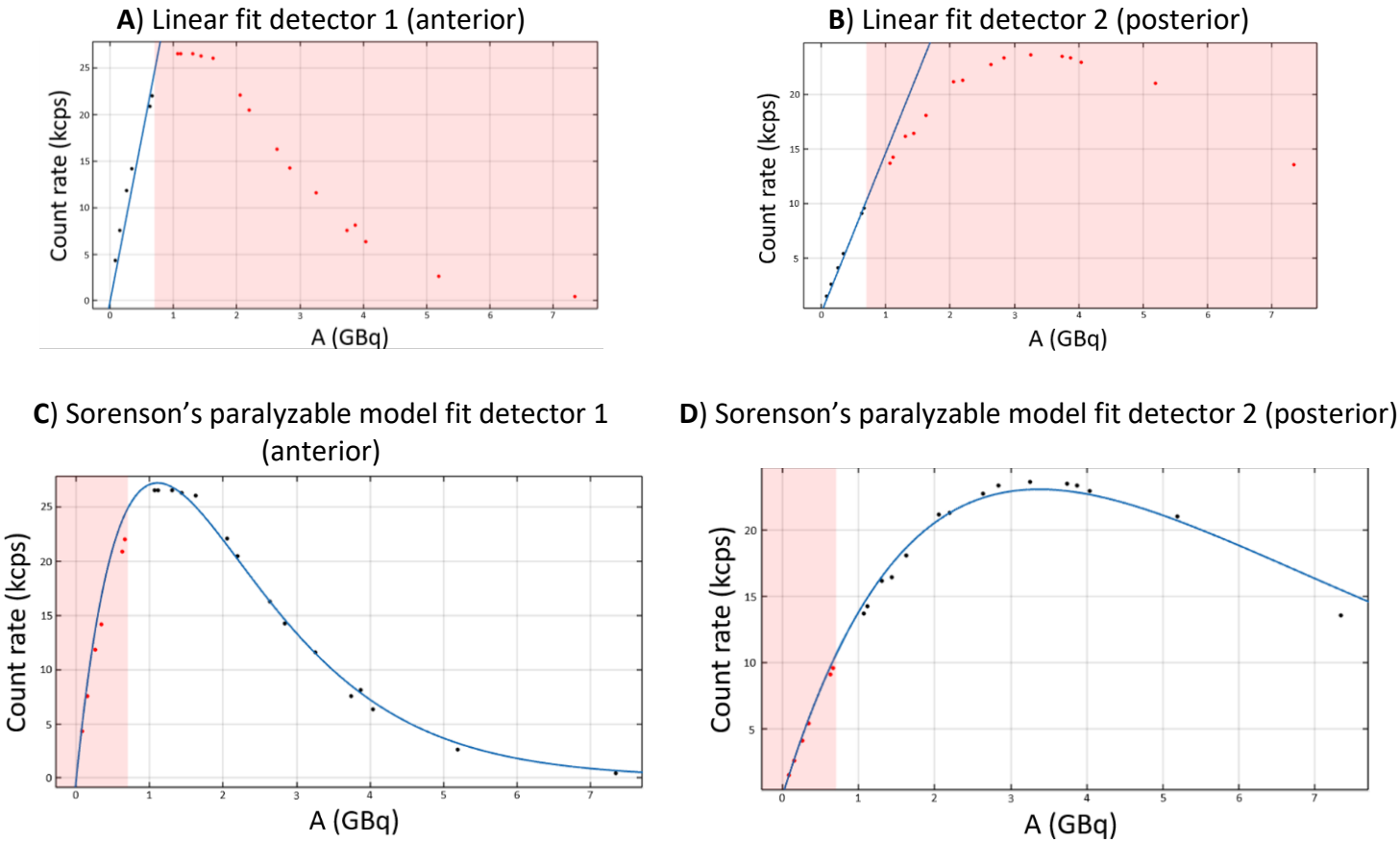

Figure 10. *The curve fits for the anterior and posterior detectors (units in kcps and GBq on the y- and x-axis, respectively). A and B show the linear fit through the lowest 6 measurement points. C and D illustrate the fitting of Sorenson's curve to the remaining points.*

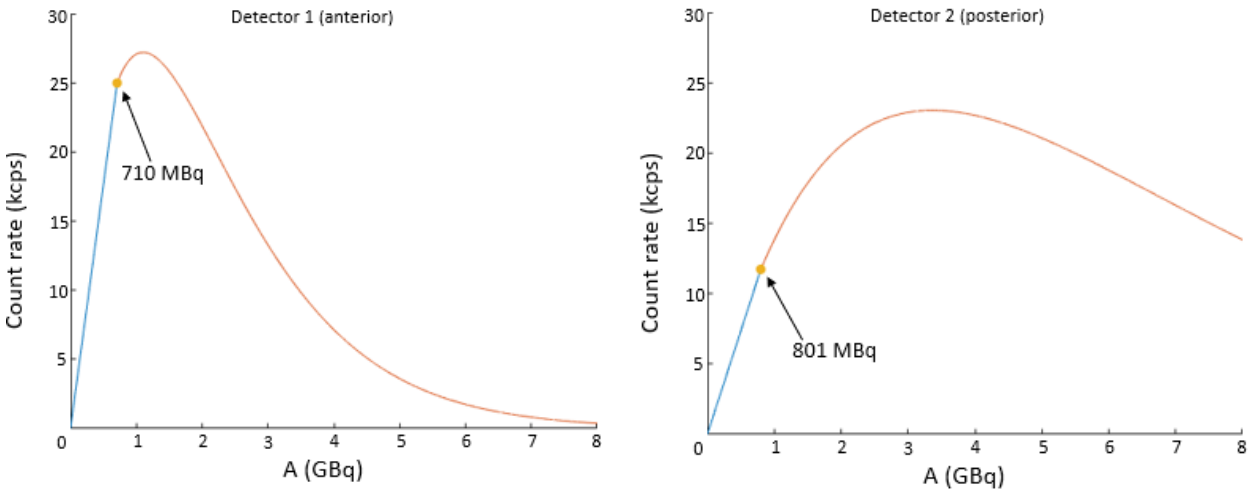

Figure 11. *The linear- and Sorenson's fitted curves were stitched together at their point of intersection, to develop the calibration curves of this SPECT system.*

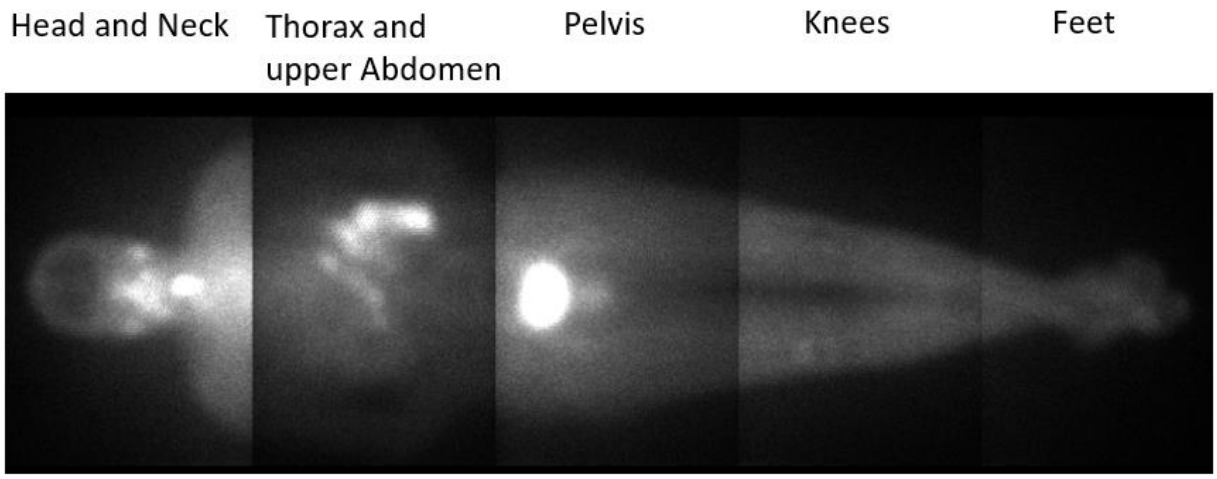

Figure 12. *The spot-views of the total body scan of a 5.7 GBq RAI-therapy patient. The spot-view containing the Thorax and upper Abdomen (2nd from left) is darker compared to the other spot-views.*

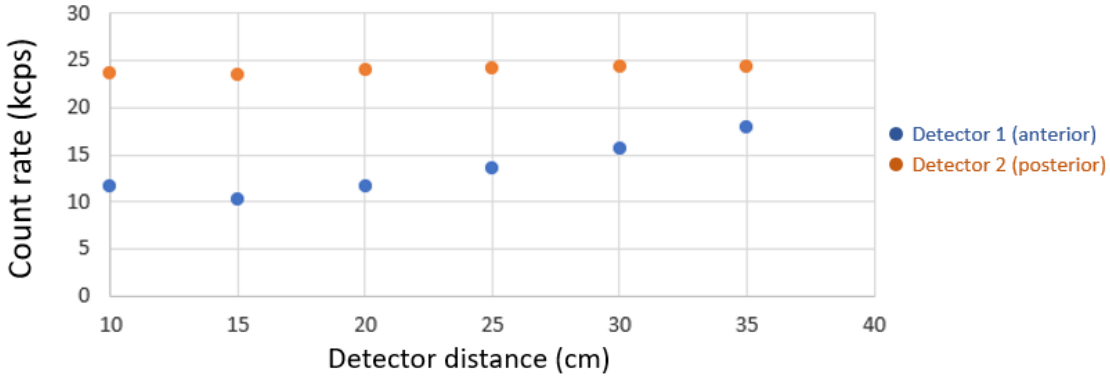

Figure 13. *The results of the 6 measurement with varying distances between the detector and the phantom containing a 3.4 GBq I-131 capsule.*

Part I: Discussion and Conclusion

Uniformity I-131

Although only 4 measurement points were acquired using tomography with the SPECT/CT system, the available data suggest the gamma camera should be uniform across the detector elements and linear with lower ACs. The linearity shows dead-time effects played no role in the quantification for this experiment.

Dead-Time Characteristics

The high R^2 for the linear and Sorenson fits indicate good accuracy and precision of the 21 point-source measurements. Detectors 1 and 2 showed different cutoff points after which dead-time effects were observed. These values (lowest cutoff at 710 MBq) indicate dead-time effects can impact quantification quite significantly, given the common administered therapeutic quantities of up to 7.4 GBq. The difference in the curves between the anterior and posterior detector is most likely explained by a combination of factors. First, while the simulation of the thyroid in the neck is also a strength of this phantom, as a result the I-131 capsule was placed closer to the anterior detector. This results in less attenuation of the gamma photons through the phantom itself for the anterior measurements. Second, the scanner bed was present between the phantom and the posterior detector, resulting in more distance, attenuation and scatter, compared to the anterior detector. The difference between the detectors was a used as an advantage due to the paralyzable behavior of the gamma cameras in the non-linear range, which always yield two possible activities when used as a calibration curve. The peaks of both detectors do not overlap and can be used as a reference when trying to calibrate a count rate measurement, which was attempted for a whole body patient scan.

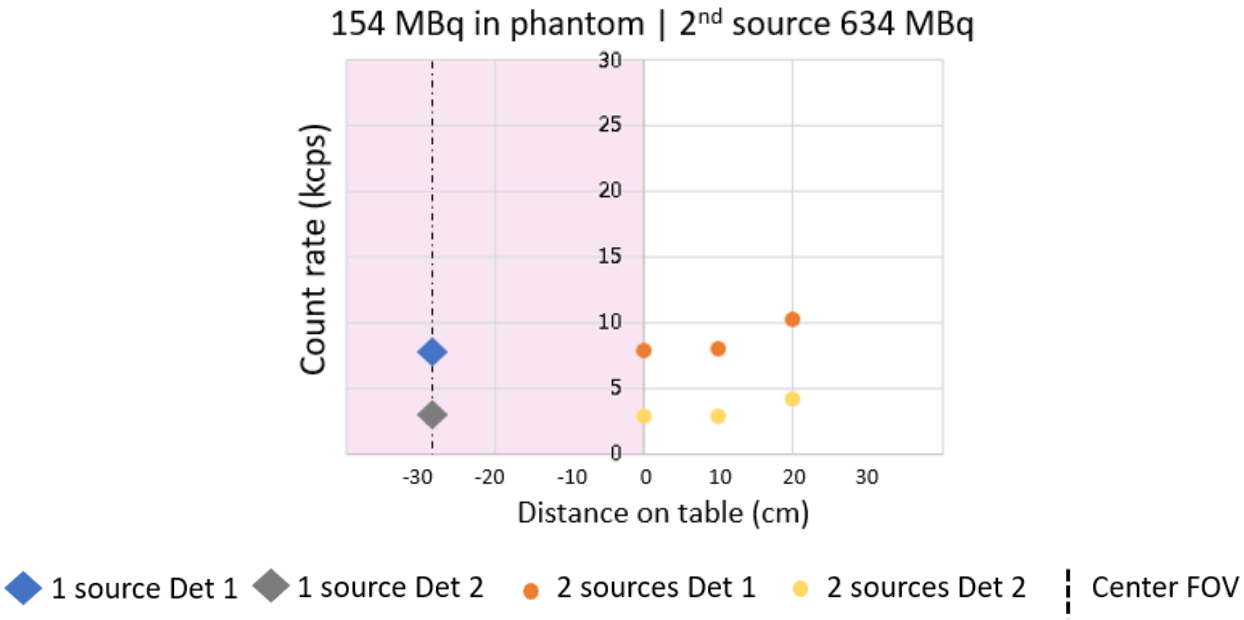

Figure 14. *Experiment 1 of the FOV experiments in which a 154 MBq I-131 capsule was placed in the center of the FOV and a 634 MBq I-131 capsule was placed outside the FOV to test outside influence on the measurement. The purple plane indicates the FOV and the dashed line shows the FOV center.*

Patient Total Body Scan

The accuracy of the simple geometry of the point-source measurements did not represent the more complex geometry and distribution of activity in the patient. The activities found in the spot-views of the whole body patient scan, using the curves, were inaccurate and inconsistent between the anterior and posterior detectors. There are factors that make dead-time correction complex in clinical application. First, this model lacks a method to account for attenuation and scatter through the different tissues of the patient. Attenuation correction is widely applied in both SPECT/CT and PET/CT, in which the CT scan is used as an attenuation map. Scatter correction could be applied with triple energy window correction. Visually, the dead-time effects were observable in the spot-view of the patient's thorax/upper abdomen, where it is assumed the capsule was still largely present in the stomach.

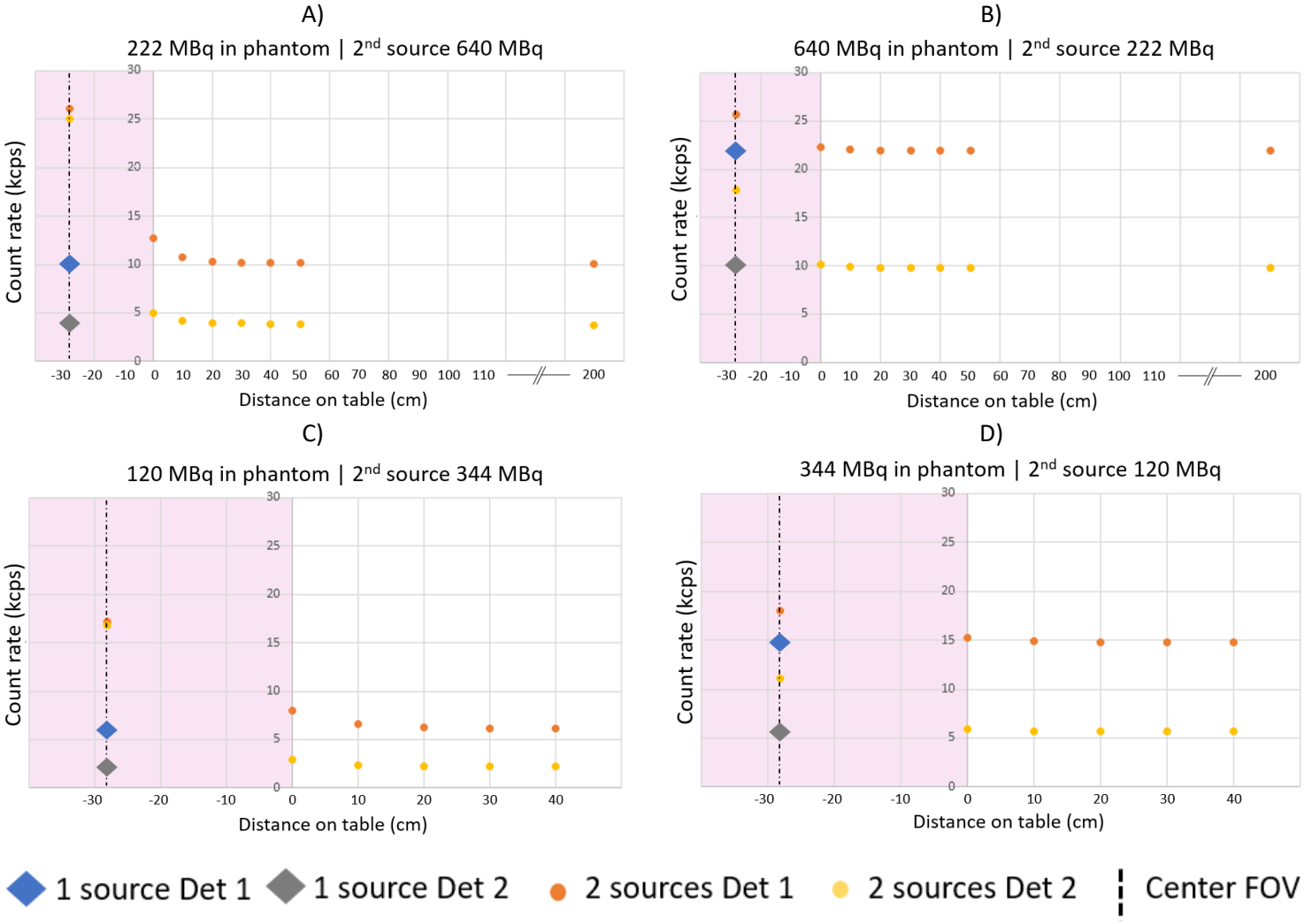

Figure 15. *A and B show the results of experiement 2 of the FOV experiments. The phantom contained a 222 MBq I-131 capsule and a 640 MBq capsule was placed outside the FOV at varying distances. The purple plane indicates the FOV and the dashed line shows the FOV center. The position of the capsules was switched next. C and D illustrate experiment 3, in which the measurements were repeated with a 120 and 344 MBq I-131 capsule.*

Therefore, this spot-view likely contained most of the total activity. It shows a darker BG compared to the other spot-views, indicating the detectors were saturated. It was assumed the amount of activity present in the spot-view of the feet was comparatively low and in the linear range. Thus, it was assumed dead-time effects played no role in this spot-view. Therefore, an alternative method of dead-time correction might be applied in this patient, in which the BG of each spot-view is scaled to the BG of the feet, providing correction factors.

A CT-scout was available for the patient from this report. Preliminary results of CT-scout attenuation correction and the alternative dead-time correction indicate a similar estimation of 6.9 GBq. However, more investigation and patient scans would be needed to validate this new approach. Scatter correction was not included yet. Alternatively, other measurement equipment should be investigated and compared, such as the use of smaller dose rate meters.[58,59] For whole body activity measurements, it is not important to know how the activity is distributed. This suggests that a consistent dose rate meter, that might be less affected by dead-time effects up to 7.4 GBq, could be used instead of SPECT for the purpose of whole body dosimetry.

Geometry and Field of View

The results of the experiment in which the detector-phantom distance is varied (Figure 13), suggests the count rate increases with larger distances. This might feel counter-intuitive, given a dose rate should decrease quadratically with distance. This phenomenon might be explained because of dead-time effects. The capsule activity used in this single experiment was outside the linear range. Therefore, the detectors were saturated. The logic of the quadratic law could still be applied, as the increased distance caused less saturation, which in turn increased the measured count rate. Repetition of this experiment, with I-131 activities in the linear range (<710 MBq), would be needed to truly assess the effect of detector-source distance in planar SPECT dosimetry.

With the FOV experiments, the first experiment (Figure 14) is an outlier compared to the latter two FOV experiments. An increase in count rate was observed the further a second radioactive source was moved from the FOV. The combined activity of the two sources was 788 MBq, implying dead-time might again be the cause of this count rate increase. However, in experiment 2 a higher combined activity of 862 MBq was used and the result was the opposite; a decrease in count rate. The results of experiments 3 were consistent with experiment 2, which lead to the assumption an unknown inconsistency during the physical measurement or in the processing occurred. FOV experiments 2 and 3 contained more measurement points as well and should therefore be considered closer to reality than experiment 1. All FOV experiments confirm that activity outside the FOV can influence quantification and contribute to dead-time effects with high quantities. This is likely to have occurred in the whole body scan of the patient as well. A solution or alternative measurement method with a large FOV is needed.

Comparison with Literature

Dead-time has been characterized in similar phantom studies with I-131 for multiple SPECT/CT systems. Gregory et al. reported losses in counts due to dead-time effects at 1.6 GBq with the Discovery system, which is significantly larger than the 710 and 801 MBq observed here.[48] However, a vendor-specific 'fast mode' was used in this study. This 'fast mode', which was developed by GE to enable accurate quantification for high count rates with the isotope Tc-99m, is still a black box, which was unavailable to us as it deleted the energy window settings each time. Furthermore, as described in literature and as supported by Part I, the level at which losses occur due to dead-time effects vary depending on object geometry, attenuation, the crystal thickness and

type of collimator.[48,53] If these factors are consistent and simple, the accuracy is consistent. For use in the clinic, little literature on whole body quantitative SPECT with I-131 exists. Dead-time correction was investigated in patients for Lu-177-SPECT/CT, after phantom experiments, where dead-time correction factors improved accuracy to 2.6% with high activities, which is 8.5 times more accurate compared to our 22%.[60–63] In most studies that used SPECT/CT with therapeutic quantities of I-131, whole body scans were often performed 2-7 days post-administration at the earliest, to avoid dead-time effects.[64–66] In the clinic, I-131 scintigraphy is also performed around 7 days post-administration, partially for the same reason (iodide accumulation over 7 days also results in higher diagnostic sensitivity with I-131 scintigraphy).[67] For now, the literature suggests to avoid dead-time effects with I-131 SPECT/CT, if possible.

Clinical Interpretation

In the general introduction, bone marrow/blood AD and whole body retention toxicity limits at 48 hours during RAI therapy were mentioned. In practice, it hardly occurs that a patient exceeds these limits with typical activities of 3.7-7.4 GBq, unless the patient has impaired kidney function without renal replacement therapy and/or is severely affected by lung metastases. Therefore, the clinical value of accurate intra-therapeutic blood and whole body toxicity measurement methods in the general population can be argued for typical therapeutic activities. Furthermore, if the personal MTA can accurately be predicted with pre-therapeutic dosimetry for a patient, there should be no need to validate the predicted MTA in an intra-therapeutic setting, unless significant changes in iodine biokinetics occur between pre-treatment and intra-treatment, such as kidney deterioration and increased iodine, TSH and/or thyroid hormone load. With the use of lower quantities of (I-124) activity for MTA prediction, dead-time effects play no relevant role. Higher RAI activities than in the current practice could be administered in the future if MTA predictions are accurate. To validate MTA prediction with I-124, accurate intra-therapeutic validation with high I-131 activities is still required. To measure toxicity limits within 24 and 48 hours, a solution to dead-time effects is still necessary for accurate intra-therapeutic quantification. Only toxicity dosimetry was investigated in this report. To determine the response of lesions to an AD, intra-therapeutic lesion dosimetry is needed. In addition to dead-time effects, PVE is an additional important factor for which RCs for I-131 SPECT/CT need to be determined, as will be described in Part II, although for I-124 PET/CT.

Conclusion

In conclusion, dead-time effects are consistent with simple geometry in planar scintigraphy. However, quantification of high I-131 quantities was inaccurate in a clinical setting, due to dead-time effects combined with a lack of attenuation correction. At least one more patient should be included for comparison. For accurate intra-therapeutic dosimetry in early time points, further investigation is needed into the preliminary attenuation and scatter correction methods proposed by this study, the use of measurement equipment that is less sensitive to dead-time effects, possibly such as dose rate meters.

Part II: Lesion Dosimetry with I-124 PET/CT

Part II: Aim and Hypothesis

The Omni Legend (32 cm); GE Healthcare, is the recently acquired digital PET/CT system in the LUMC as of spring 2023. The standardized phantom experiments described in the EARL program are the ideal first step towards validation of this system for lesion dosimetry with I-124. However, as mentioned in the general introduction, no EARL accreditation program exist for I-124. Therefore, the following research question should be investigated:

How accurate and precise is the Omni Legend for pretherapeutic lesion dosimetry with I-124 in differentiated thyroid cancer determining how does this relate to the EARL requirements for F-18.

For F-18, key requirements are proposed by EARL. First, the difference in calibration measurements for a known uniform I-124 AC should be ≤10%, between the PET/CT system and a validated dose calibrator.[68] Second, a PET scan of a uniform AC should be within acceptable noise limits, i.e. a coefficient of variation (COV) ≤15%. Finally, the EARL website presents F-18 RC limits for 6 lesion sizes with diameters between 10 and 37 mm.[69] The hypothesis is that a recovery curve fitted to these RCs should illustrate a sharp decrease in smaller volumes, as demonstrated in Figure 16. The following aims are set for Part II.

2.1 Determine quantification accuracy and coefficient of variation for homogenous I-124 activity concentrations.

2.2 Determine accuracy and precision of recovery coefficients for pre-therapeutic I-124 activity concentrations in thyroid lesions.

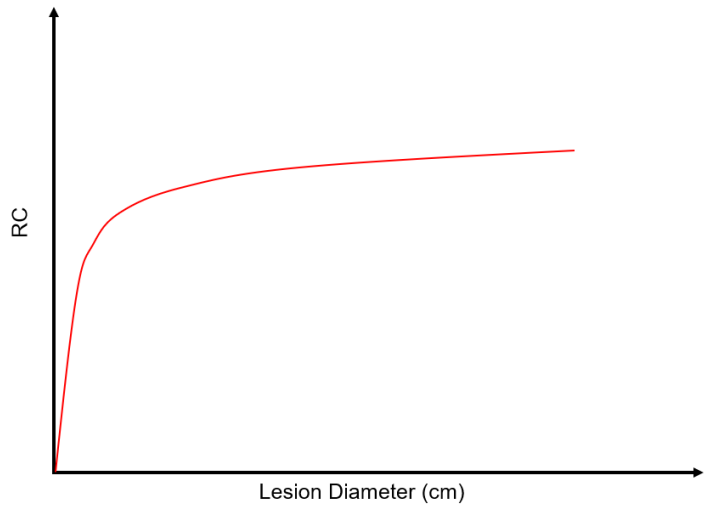

Figure 16. *The hypothesized recovery curve behavior of a PET system, due to partial volume effects. Activity measurements in lesions with a small diameter tend to be underestimated, resulting in decreased recovery coefficients (RC).*

Part II: Methods

Uniformity I-124

A cylindrical uniformity phantom was measured to achieve aim 2.1. In compliance with the EARL accreditation tests for F-18, the uniformity phantom (6,726 mL) was filled with a sodium iodide I-124 solution containing 67.25 MBq, giving an AC of 9.82 kBq/mL at the time of acquisition.[68] A validated dose calibrator (VIK-202; Comecer) was used to measure the activity given to the phantom. One PET/CT acquisition was made using 2 bed positions and 5 minutes per bed position, as recommended in the EARL requirements. The local EARL1 reconstruction parameters for F-18-FDG were applied. [70] Vue Point HD, which is an OSEM-based iterative reconstruction algorithm was used.[71] The parameters were 3 iterations, 22 subsets, 3.65×3.65 mm pixel size (192×192 matrix), 2.07 mm slice thickness, CTAC, scatter correction, 7 mm full width at half maximum Gaussian filter, branching correction and decay correction. PMOD was used to place a spherical and cylindrical VOI with a diameter (and height) of 15 cm in the center of the phantom in the PET-scan of the phantom.[68,72–75] The mean AC (±SD) was determined in both of these VOIs. The $RC_{uniformity}$ was calculated by dividing the mean AC with the true AC.

Recovery Coefficients – Phantom Preparation

To achieve aim 2.2, phantom experiments were performed with I-124 on the PET/CT system on a single day. The National Electrical Manufacturers Association (NEMA) Image Quality phantom was used. The NEMA phantom contains a cylindrical lung insert and six spherical inserts that represent lesions, with diameters of 10, 13, 17, 22, 28, and 37 mm. An illustration of this phantom is provided in Figure 17. The spheres of the NEMA phantom were filled from a 500 mL stock solution containing 20.79 MBq of sodium iodide I-124, resulting in an AC of 41.58 kBq/mL. This value falls in the range of ACs observed in DTC metastases and ACs used in other phantom studies.[76–79] The dose calibrator was used to measure the true activity administered to the NEMA phantom spheres, NEMA phantom BG and residual activity in syringes and vials.

The AC in the BG (9,833 mL) of the NEMA phantom was varied to create different BG-to-spheres ratios of 1 to infinity, 1 to 500, 1 to 125 and 1 to 10. This was done to compare the accuracy of AC quantification in lesions across varying degrees of BG-to-sphere contrasts, i.e. radiation spill-in, as the BG-to-lesion ratio is variable in metastatic DTC lesions and depends on lesion and surrounding tissue uptake behavior.[76] Theoretically, non-thyroid BG tissue, that does not express NIS, should not show avidity to iodide. This is generally confirmed in the clinic, where DTC

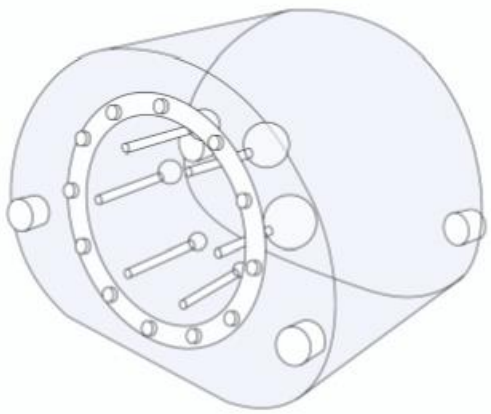

Figure 17. *The NEMA phantom with spherical insets.*
Image from: Westerbergh et al [50]

lesions tend to be highly focal. Comparable phantom studies have used ratios between 10 and 750 and confirm the observations of high contrast ratios for DTC lesions.[78,80–85] This provided the rationale for the ratios used in this experiment. Additionally, the 1 to 10 ratio is required for F-18 EARL accreditation. The 1 to infinity ratio also serves as a reference, in which there is no spill-in caused by radioactivity present in the BG. The BG of the NEMA phantom was filled with distilled water for 1 to infinity, after which gradually I-124 was added to create each ratio.

Recovery Coefficients – Acquisition and Reconstruction

For each BG-to-sphere ratio, 5 PET/CT acquisitions were made to assess the precision of AC quantification in lesions, giving a total of 20 NEMA phantom acquisitions. The NEMA phantom was repositioned between each acquisition to simulate variation in lesion edge locations with respect to the post-reconstruction image volume matrix voxel borders. Furthermore, 2 bed positions were used in all acquisitions to ensure a sufficient homogenous axial sensitivity across the phantom, as compliant with EARL. For the 1 to infinity ratio, the first acquisition was made with high count statistics by using 20 minutes per bed position, to serve as a baseline. The acquisition duration was dependent on the amount of activity in the NEMA BG and was increased or decreased to account for lower or higher count statistics, respectively. Acquisition durations were increased by the percentage of decay, if relevant. For the 1 to 10 ratio, which is required for F-18-FDG EARL accreditation, the standard clinical acquisition protocol for F-18-FDG was applied, which uses 2 minutes per bed position. The acquisition duration times for the NEMA experiments are summarized in Table 2. The local EARL1 reconstruction parameters for F-18-FDG were applied. Vue Point HD, which is an OSEM-based iterative reconstruction algorithm was used[71]. The parameters were 3 iterations, 22 subsets, 3.65×3.65 mm pixel size (192×192 matrix), 2.07 mm slice thickness, CT-based attenuation correction, scatter correction, 7 mm full width at half maximum Gaussian filter, branching correction and decay correction.

Recovery Coefficients – Data Analysis

The RCs were calculated in PMOD. The ACs were determined in the BG of the NEMA phantom and in each sphere, for each PET-scan. The AC_{BG} (±SD) was determined by taking the average of a VOI consisting of 12 cylinders with a diameter of 15 mm and a height of 168 mm, spread evenly throughout the BG, away from the spheres, lung insert and phantom edges. The COV of the BG was calculated by dividing the SD by the AC_{BG}, multiplied by 100%. VOIs were drawn over each sphere to determine: the AC_{mean}, defined using a 50% BG corrected isocontour; and the AC_{max}, defined as the maximum voxel value in a sphere.[69] The ratio of the measured AC and true AC provided the RC_{BG} in the NEMA phantom and the RC_{mean} and RC_{max} for each sphere. In total, there were 15 RC_{BG} (excluding the 1 to infinity ratio due to division by 0), and 120 RC_{mean} and RC_{max} (20 RC_{mean} and RC_{max} per sphere). In 3 acquisitions of the 1 to 125 ratio and all 5 acquisitions of the 1 to 10 ratio, F-18 was selected as the isotope in the acquisition protocol instead of I-124 due to human error. This caused an undercorrection for branching (the positron-emission yield of the isotope) and an overcorrection for decay during acquisition, in the reconstruction, given the branching of 0.23 vs 0.97 and the half-life of 100.22 vs 1.83 h for I-124 and F-18, respectively.

TABLE 2

Setup of the NEMA phantom experiments, with activity concentrations (AC) in the NEMA phantom and its background (BG), per BG-to-sphere ratio

True BG-to-sphere ratio	AC spheres (kBq/mL)	AC BG NEMA (kBq/mL)	Acquisition duration per bed position (minutes)	Decay at time of acquisition (%)
1:infinity	40.32	0	4 (1 acq. with 20)	1
1:509	39.88	0.08	4	2
1:153	39.55	0.26	1:05	3
1:10	39.36	3.94	2	3

A manual correction was applied to the RCs for these 8 acquisitions, by multiplying them with the ratio of the branching factors (4.22) and the ratio of the remaining percentage of activity of both isotopes, after half of the total acquisition duration (duration of one bed position). This decay correction is an approximative approach based on the assumption of near linear decay behavior within the relative short acquisition times, compared to the half-lives of both isotopes. The obtained RC_{mean} and RC_{max} were averaged per BG-to-sphere ratio and compared to the EARL1 F-18 RC limits.[69] For application in lesion dosimetry, RCs for a continuous range of lesion size is needed, in addition to only the discrete NEMA sphere diameters. Therefore, RC measurements were fitted with

$$RC(V) = \alpha(1 + \left(\frac{\gamma}{V}\right)^{\beta})^{-1} \quad \text{Eq 8)}$$

Where V is sphere volume in milliliters and α, γ and β are fit parameters.[53,76] The NEMA sphere diameters (in cm) were converted to sphere volumes (with $V = \frac{4}{3}\pi r^3$). A NonlinearLeastSquares Trust-Region algorithm was used in MATLAB CurveFitter to fit a mean and max recovery curve with Equation 8, using all 120 RC_{mean} and 120 RC_{max}, respectively. The mean (±SD) RC_{mean} and RC_{max} were calculated per sphere volume, using all 20 measurements across all BG-to-sphere ratios.

Part II: Results

Uniformity Phantom I-124

The mean AC (±SD) determined from the spherical and cylindrical VOIs with a 15 cm diameter (and 15 cm height) were 11.64 (±0.69) and 11.61 (±0.70) kBq/mL, respectively. The RC_{uni} in these VOIs were 1.19 and 1.18, respectively. This is more than a 10% systematic bias between PET and the dose calibrator.

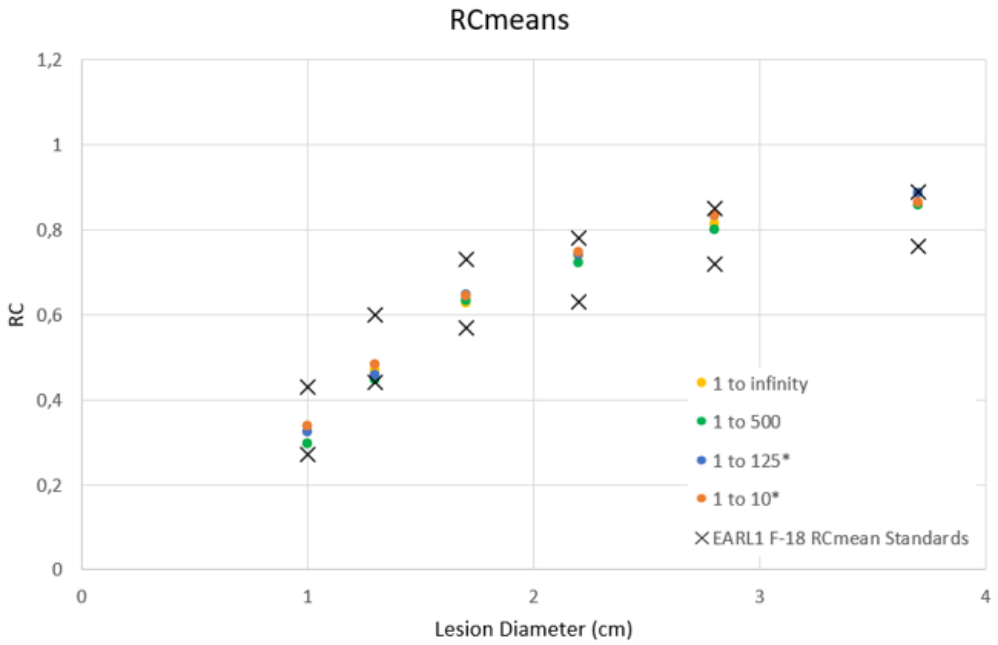

Figure 18. *The average RCmean for each sphere of each BG-to-sphere ratio experiment. The spheres (lesions) are presented on the x-axis as their diameter. The RCs are on the y-axis. The EARL1 RCmean standards (lower and upper limits) are represented as an 'X' for each sphere. *A manual correction for branching and decay of I-124 was applied to RCs obtained from acquisitions and reconstructions with F-18 as selected isotope.*

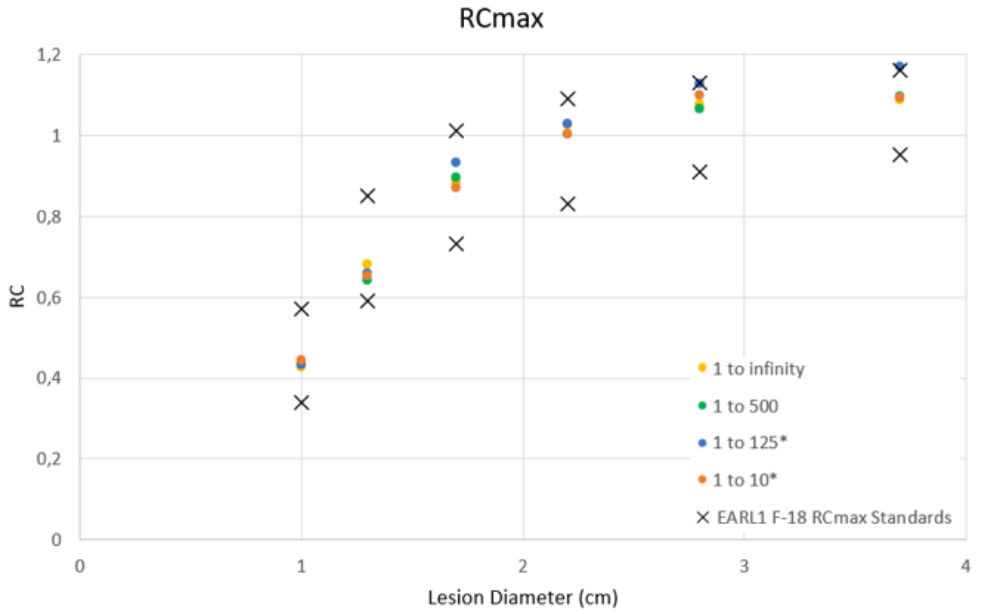

Figure 19. *The average RCmax for each sphere of each BG-to-sphere ratio experiment. The spheres (lesions) are presented on the x-axis as their diameter. The RCs are on the y-axis. The EARL1 RCmax standards (lower and upper limits) are represented as an 'X' for each sphere. *A manual correction for branching and decay of I-124 was applied to RCs obtained from acquisitions and reconstructions with F-18 as selected isotope.*

Recovery Coefficients

Visual assessment of the phantom scans revealed a high uptake region in the absorption mat underneath the phantom, indicating leakage of F-18 from phantom experiments conducted prior to the experiments presented here. The mean RC_{BG} (COV%) in the BG of the NEMA phantom was 1.10 (14.81%), 2.11 (47.78%) and 1.72 (56.05%) for the 1 to 10, 1 to 125 and 1 to 500 ratios, respectively. This further confirms a larger than 10% error between the PET/CT system and the dose calibrator. For the 1 to infinity ratio, an AC_{BG} of 0.04-0.1 kBq/mL was measured across the 5 acquisitions. For each contrast ratio the average RC_{mean} is plotted in Figure 18 and the average RC_{max} is plotted in Figure 19.

The average RC_{mean} and RC_{max} for the largest sphere are presented per BG-to-sphere ratio in Table 3. For the 1 to infinity ratio, the largest SD in RC_{mean} and RC_{max} across acquisitions within this ratio was ±0.02 and ±0.03 (both for the 17mm sphere), respectively, including the acquisition with 20 min.

The fitting of the recovery curves yielded

$$RC_{mean} = 0.9132(1 + \left(\frac{1.078}{V}\right)^{0.908})^{-1}$$

and

$$RC_{max} = 1.142(1 + \left(\frac{0.8337}{V}\right)^{1.103})^{-1},$$

Where V is lesion volume in milliliters, with an R^2 of 0.99 and 0.98, respectively. The recovery curves are illustrated in Figure 20.

Part II: Discussion and Conclusion

Main Implications

The I-124 PET/CT acquisition overestimated the AC in the uniformity phantom, with an unexpectedly large RC (1.18) in cross-calibration with the dose calibrator. This does not meet the EARL requirement of ≤10% discrepancy (i.e. 0.90≤RC≤1.10). In the 1 to 10 ratio of the NEMA phantom, both the RC_{BG} (1.10) and COV (14.81%) were just within EARL limits. Comparatively, for the 1 to 125 and 1 to 500 ratios, the RC_{BG} (2.11 and 1.72) and COV (47.78 and 56.05%) were significantly larger. The lower counts statistics due to shorter acquisition durations partially explains the increased COV, compared to the 1 to 10 ratio. Nevertheless, these findings were unexpected and suggest either that the measurements were (to some extent) impacted by prior leakage of an F-18 phantom and/or that low I-124 ACs might be especially difficult to accurately quantify with PET. Given the rationale to use low activities for pretherapeutic I-124 dosimetry, explanations, solutions and/or optimization need to be found and measurements need to be repeated to confirm or rule out current findings.

TABLE 3

Average recovery coefficients (RC) per background-to-sphere ratio

Ratio	**Average RC_{mean}** (±SD) **largest sphere**	**Average RC_{max}** (±SD) **largest sphere**
1 to infinity	0.86 (±0.01)	1.09 (±0.02)
1 to 500	0.86 (±0.01)	1.09 (±0.02)
1 to 125*	0.89 (±0.01)	1.17 (±0.02)
1 to 10*	0.86 (±0.01)	1.09 (±0.02)

**A manual correction for branching and decay of I-124 was applied to RCs obtained from acquisitions and reconstructions with F-18 as selected isotope.*

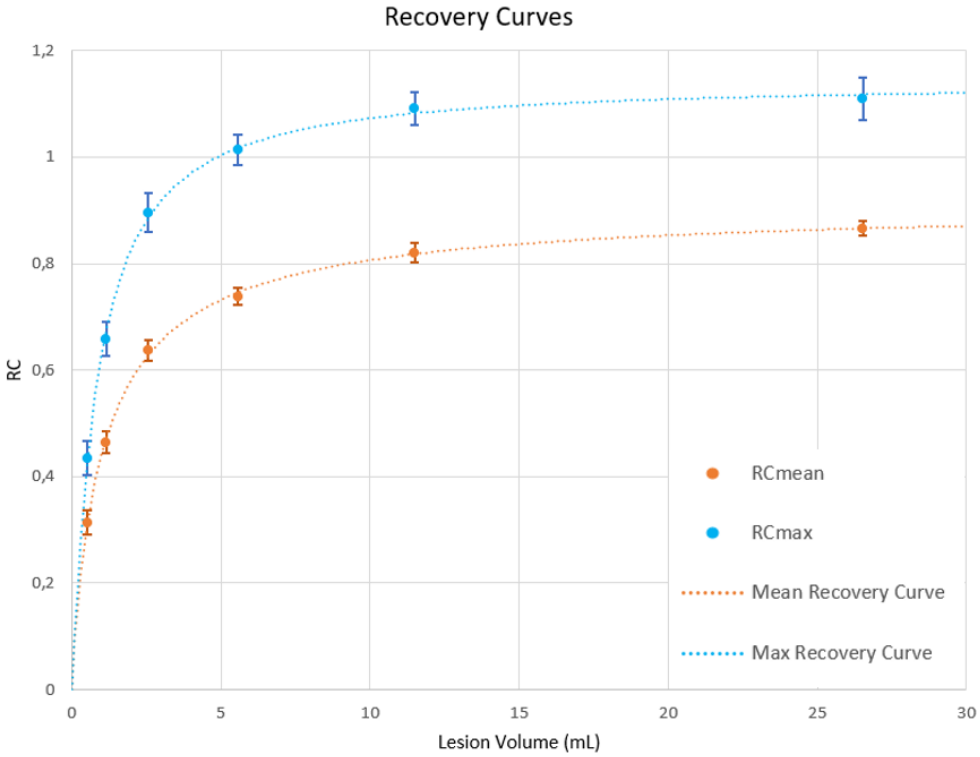

Figure 20. *The recovery curves (dotted lines) that were fitted to all 120 RCmean and 120 RCmax.. The points on the curves are the mean (±SD error bars) of the 20 measurements per sphere volume. The sphere diameters have been converted into sphere (lesion) volumes (mL) for the fitting of the recovery curves, which is represented on the x-axis. The RCs are on the y-axis.*

The RC_{mean} and RC_{max} for the spheres were within EARL1 F-18 limits for all BG-to-sphere ratios, indicating high accuracy. The low SDs observed between and within BG-to-sphere ratios indicate high precision, despite the impact of the overestimated BG on the isocontour VOI for RC_{mean}, especially for the lower BGs. This implies the F-18 EARL acquisition and reconstruction protocol can be applied to I-124 dosimetry to achieve an accuracy and precision comparable to the F-18 EARL standards. Whether the RC_{mean} and RC_{max} have also been overestimated, as with RC_{BG}, cannot be adequately assessed due to the PVE affecting the former two and hardly affecting the larger subvolumes used to determine the latter. However, the AC in the spheres was relatively high, which implies the overestimation might be limited. Therefore, these RCs can be applied in the RESET study. Low predicted ADs in lesions (i.e. ≤1 Gy) might be overestimated with a maximum factor of 2.11, compared to higher predicted ADs, as a result. However, in determining whether the predicted AD is above or below the threshold of 20 Gy, the impact of this overestimation may possibly be limited. Acceptable RC limits for I-124 do not yet exist to allow for comparison to a standard. Any manual correction to the overestimation may add a bias to the RCs.

Further possible explanations for the unexpected overestimation might be found in the differences between I-124 and F-18 as isotopes. I-124 has lower branching, more prompt gamma rays, and larger positron range, which inherently leads to more scatter events, random events and thus noise, when compared to F-18. Accurate quantification depends on optimized scatter correction methods to remove these false events. An axial line profile was taken through the uniformity phantom, which was uniform and ruled out that the scatter correction algorithm was the cause of the overestimations. Possible unnoticeable errors can occur during the administration of activity to the phantom, dose calibrator measurements and the selection of the acquisition and reconstruction parameters. The dose calibrator was calibrated prior to the phantom acquisitions and samples taken from the NEMA phantom BGs were measured in a calibrated well counter, which further indicated the dose calibrator was accurate. Sources of radiation that might unintentionally have been present near/in the PET/CT-scanner could also be a factor, such as the prior F-18 leakage. Another possibility is that unintended errors may have occurred in using PMOD for analysis, which can be ruled out by comparing analysis with different software. This report recommends foremost to repeat the experiments described in Part II, to allow for comparison with current results and rule out any systematic errors with I-124 quantification with the Omni Legend. If the overestimation persists in repeat measurements, potential causes should be ruled out systematically, starting with the reconstruction algorithm, by comparing with older reconstruction methods such as filtered back projection.

Comparison with Literature

A study by Jentzen et al. also found an overestimation (8%) in homogenous AC BG measurements with I-124 PET/CT, using a cylindrical uniformity phantom.[80] Other studies support their explanation that prompt gammas are the most important cause of this overestimation and also found that use of their vendor-specific prompt gamma correction methods improved accuracy.[78,83] However, the overestimation found in these experiments was 10% greater compared to Jentzen at al. For the NEMA spheres, RC_{means} found for the largest sphere in other studies range between 0.63-0.87.[76,81,84,85] This would place the RCs in this experiment near the higher RCs observed with I-124 studies. The Omni Legend is part of a new generation of PET scanner hardware and reconstruction software. Therefore, higher sensitivity and resolution, resulting in higher RC compared to the literature, may be expected. However, it should be taken into consideration that

the PET/CT system currently may have overestimated the AC in the spheres, as it did in the homogenous BG.

Strengths and Weaknesses

The main strength in the designs of these experiments is the standardization and widespread use of EARL, which allows for comparison with (future) European-wide I-124 phantom studies. Another strength is that there are 5 acquisitions per multiple clinically representative BG-to-sphere ratios, which provided a sufficient amount of data to assess precision. The first weakness is the F-18 leakage on the absorption mat. In future experiments, the absorption mat should be replaced more often, especially between experiments with different isotopes. The total experiment was only performed once on a single day. Furthermore, the manual correction of the acquisitions that were set to the wrong F-18 isotope, which introduced a systemic bias to the results of the RC spheres for the 1 to 125 and 1 to 10 ratios. In lower ACs, the scatter and random event correction might cause more voxels with negative ACs. The VPHD reconstruction algorithm could apply overcompensation when a significant amount of negative AC voxels are encountered. However, this is speculation and different reconstruction methods should be applied to verify this. Improved prompt gamma correction, point spread function modelling, or non-iterative reconstruction methods (filtered back projection) could either increase accuracy or identify limitations in the applied reconstruction and/or acquisition settings. Different reconstruction methods and parameters were not investigated or were not available yet.

Conclusion

Hence, there is uncertainty regarding the accuracy of the RCs for I-124 in DTC lesions for the new digital PET/CT system. With recovery correction using these RCs, application of Equation 1 for dosimetry will likely result in an overestimation of the AD in DTC lesions, especially in low ACs. In the worst case in the clinic, this could lead to patients being labelled as unrefractory and to overtreatment with RAI, in undifferentiated refractory patients who were scanned on this system. However, with the knowledge of the maximum overestimation (factor 2.11) and when comparing to a threshold of 20 Gy, lesion dosimetry on study patients can, with consideration, be recommended with the Omni Legend, especially if the predicted AD << 20 Gy or >> 20 Gy. Accuracy and precision are sufficient (within EARL limits) for high ACs. Nevertheless, it is recommended to rule out causes of measurement error systematically, starting by repeating the experiments in Part II.

General Discussion

In this report, the quantitative accuracy and precision of contemporary SPECT and PET/CT were investigated in Part I and Part II, using phantom experiments to simulate measurements performed in intra-therapeutic toxicity dosimetry and pre-therapeutic lesion dosimetry in thyroid cancer, respectively. In this general discussion an overview of the possible implications of the findings from these experiments and perspectives for future research are presented.

Part I

A model was developed in Part I to correct for the dead-time effects in intra-therapeutic SPECT dosimetry. Despite good accuracy and precision with simple geometry in a phantom, dead-time effects appeared to be more inconsistent in a patient than can be corrected for by our simple model, with typical I-131 activities (3.7-7.4 GBq). For future research, at least on more patient should be included to test the model again and further investigation is needed into the preliminary attenuation and scatter correction methods in the current model and the use of measurement equipment that is less sensitive to dead-time effects, possibly such as dose rate meters. Intra-therapeutic toxicity dosimetry may hold more scientific than clinical relevance, as a therapeutic activity has already been determined and administered in this stage and intra-therapeutic toxicity hardly occurs. However, to investigate the value of predictive pre-therapeutic toxicity dosimetry, which is needed to determine the MTA, accurate intra-therapeutic validation is still required.

Part II

In Part II, low homogeneous BG ACs were overestimated in pre-therapeutic I-124 PET/CT phantom experiments, possibly in part due to a measurement error. Other potential causes of overestimation might have originated in the system hardware, reconstruction algorithm, phantom preparation process, measurements and/or data analysis software. For future research, the uniformity and NEMA phantom measurements should be repeated, to assess whether the overestimation is systematic. Should that be the case, potential causes should be ruled out systematically, first starting with applying older reconstruction methods such as filtered back projection. However, the quantitative accuracy and precision for higher ACs in lesions were within EARL limits, which is of relevance to clinicians in determining the AD relative to a threshold (of 20 Gy in the RESET study). Regardless of any overestimation, low ACs in lesions are not likely to achieve an AD of 20 Gy and accuracy increases with the AC. Therefore, the RCs from Part II can be applied by clinicians.

Variability in Iodine Kinetics

The purpose of pretherapeutic dosimetry in DTC is to investigate how much I-131 activity is needed to give an AD of ≥20 Gy in thyroid lesions, without exceeding toxicity limits to radiation-sensitive organs. In the current clinical practice, fixed RAI activities are selected empirically and depending on physician experience and disease characteristics.[28] In addition to the need for accurate quantification methods, the dosimetric approach depends on similar iodine biokinetics of the patient and lesions in pre- and intra-therapy. To optimize RAI-therapy, lesion iodide uptake and retention in lesions is maximized by minimizing iodide intake through diet, thyroid hormone medication withdrawal and TSH-stimulation (in the RESET study). For consistency between pre- and intra-therapeutic dosimetry, clinicians and patients are required to keep these factor consistent in both. Iodine kinetics are highly variable and further depend on lesion characteristics such as volume, geometry, heterogeneity, radiobiological sensitivity and also on day-to-day biological variability, stunning and other unknown factors.[76,86,87] Although the clinical impact of stunning is somewhat controversial, studies that have investigated it agree that stunning should be avoided if

possible, by using low pre-therapeutic activities and administering therapeutic activities within a short period.[88–91] Furthermore, it is assumed patient and lesion biokinetics do not distinguish between the two different, yet chemically identical, iodine isotopes.

Literature Comparing Pre- vs Intra-therapeutic Dosimetry

Most studies in this field compare pre-therapeutic predicted absorbed lesion doses with intra-therapeutic lesions response and not true absorbed lesion dose. These studies observed that lesion response is correlated with higher ADs and that physicians were able to change patient management and safely increase activities in subsequent RAI therapies because of pretherapeutic findings.[41,92,93] Taprogge at al. compared predicted lesion ADs (I-123 SPECT/CT) with intra-therapeutic lesion ADs (I-131 SPECT/CT) and reported a strong correlation. They also observed significant variability in RAI uptake in lesions, within and between patients.[94]

Future Perspectives for Dosimetry

Errors can be introduced at every step in AD prediction with SPECT and PET, from the patient, dose calibrator, acquisition, reconstruction to data analysis. Data analysis involves segmentation of lesions, calculating the cumulative activity $\tilde{A}_{r_S}$ and AD using S-values. However, S-values simplify AD calculations by assuming homogenous distribution of RAI and deposited energy through a lesion, independent of geometry (or rather always assumed spherical) and size, which is not always realistic. Lesion density can be uniform and heterogeneous and the range of the beta particles from I-131 can be larger than the size of small lesions. Calculation and visualization methods for the detailed spatial distribution of AD in a lesion are increasingly being investigated, especially through voxel-based dosimetry, which accounts for tumor heterogeneity.[95–98] In this dosimetric approach, the AD is determined in each voxel of a target lesion and the contribution of radiation from surrounding voxels is considered as well. Instead of organ-specific S-values, this approach requires voxel S-values, which can be computed with attenuation information from CT and with Monte Carlo simulations of particle interactions. However, this process would be too time-consuming in the clinic. Furthermore, this approach is limited by the voxel size, which is a larger scale than the level of particle interactions in cells and tissue, although smaller than the level of organ-specific S-values. The current dosimetric approach already requires complex calculations, extra patient visits, extra acquisitions and increased quantities of iodine isotopes, compared to the current clinical practice.

Future perspectives for SPECT and PET

Quantitative SPECT/CT is mainly limited by lower resolution and sensitivity compared to PET/CT and therefore has long scanning times. New innovations in next-generation gamma cameras are incorporating ring detectors and faster AI-based reconstruction methods to decrease scanning times.[99] Use of contemporary SPECT/CT systems for quantification is still reliant on correction factors for dead-time, collimator-detector response (modelling), PVE, attenuation and scatter. Optimalization of these parameters should be further investigated to allow for absolute quantification. This is a technical and time-consuming challenge, that can best be approached through cooperation and harmonization with system vendors and other centers, as variability between different systems and clinical protocols can be significant.[100] For PVE correction and intra-therapeutic lesion dosimetry with SPECT/CT, NEMA phantom experiments are recommended as a step to accurate intra-therapeutic lesion dosimetry. The main limitation in quantitative PET/CT for I-124 are prompt gammas. Similarly, optimizing prompt gamma correction is a technical challenge, which should ideally be harmonized, as the reconstructions

provided by GE (the vendor of the PET and SPECT systems in our case) is currently still a black box.

Dosimetry with other Isotopes

Quantitative accuracy (including dead-time correction) with other isotopes, such as Tc-99m and Lu-177 with SPECT/CT, is relatively high compared to I-131.[56,61] Beauregard et al. reported a deviation of 2.6% between the dose calibrator and SPECT/CT with high Lu-177 activities (up to 12.4 GBq) in patients.[62] However, there is little harmonization in phantom experiment methodology within the literature and our methods (such as different vendors, measurement geometry, phantoms, acquisition settings and reconstruction settings), which makes a direct comparison between literature and our result difficult. Most studies used SPECT/CT tomography and either multiple or larger uniform sources instead of planar acquisitions and point sources. This method uses attenuation and scatter correction, which was lacking in our method. Isotopes that emit higher energetic photons such as I-131 (364 keV) may suffer from more collimator effects, scatter and dead-time effects in general, compared to Tc-99m (140 keV) and Lu-177 (208 keV). Standardized and validated phantom experiments are needed in the future, which may lead to higher and better understood quantification accuracy with I-131 and other isotopes. For various isotopes used with PET/CT and recently introduced Lu-177 with SPECT/CT, this standardization exists through EARL. New EARL2 standards for F-18 have been in development due to improvements in detector technology in new PET/CT systems and improved reconstruction algorithms that increase accuracy of quantification with F-18. Similar harmonized standards should be developed for I-124 as well.

Future Perspectives in NIS, TKIs and Molecular Pathways

More knowledge of iodide uptake and retention in lesions and healthy tissue, response to dose, functional NIS expression and molecular pathways involving TKIs is needed, to develop therapies that increase tumor sensitivity to RAI and to develop other therapies as well. More knowledge of the response of lesions and healthy tissue to an AD can lead to better and personalized thresholds for absorbed dose and toxicity, which may allow for safe administration of higher doses in the future. A more thorough understanding of refractoriness in lesions can lead to better definitions and classification of RAI-R disease and thus, improved strategies for patients of every RAI-R definition. Single and multitarget TKIs should be further investigated, given the promising prospect of redifferentiation therapies.

Conclusion

The technical challenges of improving acquisition and reconstruction to increase quantitative accuracy with SPECT and PET and the lack of standardization in dosimetry protocols is currently a limitation for personalized therapy in DTC. Nevertheless, precision is high with SPECT and PET and there is potential for further research to increase accuracy and clinical feasibility in both. More research and standardization is needed in RAI(-R) therapy, phantom experiments and dosimetry protocols, to develop effective personalized therapies for DTC and RAI-R patients.

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Appendix

MATLAB script count rate planar SPECT images

```
% script to read in NM images (of dead time measurement), sum images
% (counts) and read in Counts Accumulated (verification), sort these by
% time.

% J.W.T. Heemskerk & Friso Schoffelen
%% reading in DICOM Tags

root_dir='H:\I-131 fantoomdata planar';
branch_dir(1,:)={'\folder1\'}; %
branch_dir(2,:)={'\folder2\'}; %

cd(root_dir);

%% Reading in dicom information from branch-folder.
folders_analyzed=0;
scan_parameters={};
image_counter=0;
clear dead_time_results2;

% Note that each image consists of multiple (3) energy windows on 2
% detectors

for p=1:2
    cd(cat(2,root_dir,cell2mat(branch_dir(p,:))));

    foldernames=dir('0*');
    numfolders=length(foldernames);

    for k=1:numfolders
        temp_branch_dir=foldernames(k).name;
        cd(temp_branch_dir);
        filenames=dir('E*');
        file_name=[filenames(1).name]; % file 'one'
        if (file_name ~='.')
            dicom_info=dicominfo(file_name);
            folders_analyzed=folders_analyzed+1;

            test=dicomread(file_name);
            %  for 6 images I have to read in Energywindowvector,
EnergyWindowInformationSequence, DetectorVector and total counts.
            for m=1:length(dicom_info.DetectorVector)
                image_counter=image_counter+1;
                switch dicom_info.EnergyWindowVector(m)
                    case 1

E_name=dicom_info.EnergyWindowInformationSequence.Item_1.EnergyWindowName;

E_ll=dicom_info.EnergyWindowInformationSequence.Item_1.EnergyWindowRangeSequence.Item_1.Ene
rgyWindowLowerLimit;

E_ul=dicom_info.EnergyWindowInformationSequence.Item_1.EnergyWindowRangeSequence.Item_1.Ene
rgyWindowUpperLimit;
                    case 2

E_name=dicom_info.EnergyWindowInformationSequence.Item_2.EnergyWindowName;

E_ll=dicom_info.EnergyWindowInformationSequence.Item_2.EnergyWindowRangeSequence.Item_1.Ene
rgyWindowLowerLimit;

E_ul=dicom_info.EnergyWindowInformationSequence.Item_2.EnergyWindowRangeSequence.Item_1.Ene
rgyWindowUpperLimit;
                    case 3
```

```
E_name=dicom_info.EnergyWindowInformationSequence.Item_3.EnergyWindowName;

E_ll=dicom_info.EnergyWindowInformationSequence.Item_3.EnergyWindowRangeSequence.Item_1.Ene
rgyWindowLowerLimit;

E_ul=dicom_info.EnergyWindowInformationSequence.Item_3.EnergyWindowRangeSequence.Item_1.Ene
rgyWindowUpperLimit;
                end
                counts=sum(sum(test(:,:,:,m))); %
                %
dead_time_results{k,:}={temp_branch_dir,char(dicom_info.SeriesDescription),char(dicom_info.
AcquisitionTime),counts};

dead_time_results2{image_counter,:}={folders_analyzed,temp_branch_dir,char(dicom_info.Serie
sDescription),char(dicom_info.AcquisitionDate),...

char(dicom_info.AcquisitionTime),dicom_info.DetectorVector(m),dicom_info.ActualFrameDuratio
n,E_name,E_ll,E_ul,counts};
            end
        end
         cd(cat(2,root_dir,cell2mat(branch_dir(p,:))));
    end
end


%% writing results to xls file
xls_name=cat(2,root_dir,'test.xls');
sheet = ['date_month];
xls_cells={'index','Folder','Series Description','acquisition date','acquisition
time','Detector','duration(ms)','Energy Window','lower limit','upper limit',...
    'total counts'};
xlswrite(xls_name,xls_cells,sheet,'A1');

for k=1:image_counter
    location=cat(2,'A',num2str(k+1));
    xls_cells= dead_time_results2{k};
    xlswrite(xls_name,xls_cells,sheet,location); % xls_cells needs to be transposed
end
```

Verantwoording

In deze verantwoording blik ik terug op tien maanden stage in het LUMC. In deze maanden heb ik ervaring opgedaan in het werken als een professionele TG'er. Door de ervaringen die ik heb opgedaan in de kliniek, in onderzoek en op de werkvloer, heb ik kunnen leren wat mijn sterke punten en uitdagingen zijn in de rol van de TG'er. In deze verantwoording komen mijn ontwikkeling in de kliniek, als persoon en als professional aan bod.

Kliniek

Mijn tijd in de kliniek heb ik vanwege het onderwerp van mijn opdracht voor het grootste deel op één thema ingericht: schildklieraandoeningen. Ik heb dit gedaan om mijn M3-opdracht beter te begrijpen en me in dat veld te specialiseren. Ik had een aantal doelen in de kliniek:

1) **Vaardig worden in klinisch redeneren, tot het niveau dat ik met de bestaande klinische gereedschappen uit de nucleaire geneeskunde, endocrinologie en heelkunde tot de belangrijkste overwegingen kan komen bij patiënten uit de schildklier-MDO's.**

In de eerste helft van deze stage ging ik 1-2 keer per week naar de vaste endocrinologie-heelkunde en endocrinologie-nucleaire MDO's met nucleair geneeskundigen en AIOSen van onze eigen afdeling. Op deze MDO's werden de complexe schildklier(kanker)patiënten besproken. Ik bereidde zelf vroeg van te voren altijd 2-3 schildklierpatiënten uit het MDO voor, door me in te lezen in de voorgeschiedenis, onderzoeksuitslagen en radiologische beelden (PET/CT, SPECT/CT etc.). De nucleaire arts bereidde ook altijd het MDO van tevoren voor. Hierbij sloot ik aan en droeg ik mijn drie patiënten voor en liet ik die voordracht, met mijn conclusies, meteen toetsen. Vervolgens kon ik bij het MDO zelf meeluisteren naar hoe de verschillende specialisten gezamenlijk tot hun overwegingen en uiteindelijke keuzes kwamen. De eerste keren was mijn voorbereiding oppervlakkig. Het lukte bijvoorbeeld wèl om de uitslagen van onderzoeken van een patiënt te begrijpen, maar nog niet om van daaruit te komen tot de overwegingen (en de voor- en nadelen) voor de vervolgkeuzes voor de patiënt. Door dit wekelijks te oefenen kon ik daar in groeien.

In het begin stelde ik vooral laagdrempelige vragen over de klinische gereedschappen (bloedonderzoek, scans, bioptuitslagen en dergelijke). Van daaruit probeerde ik vragen te stellen over de relatie tussen al deze gereedschappen, de beperkingen ervan en welke informatie ontbreekt om de klinische overwegingen voor specifieke vervolgstappen voor de patiënt goed te onderbouwen. Een voorbeeld is dat de effecten van verstoorde schildklierendocrinologie op jodiumscans van de schildklier goed te zien kunnen zijn. Aan de hand van hormoonwaarden in het bloed, de schildklierscan en andere factoren kon een diagnose beredeneerd worden. Uitdagende situaties die ik op MDO's tegenkwam waren bijvoorbeeld als er een hoge tumormarker in het bloed zat, maar geen ziekte op een (jodium- of FDG-) scan te zien was. De vraag is dan op welke informatie je af moet gaan. Door wekelijks mijn voordracht voorafgaand aan deze MDO's te toetsen heb ik ervaring kunnen opdoen in de schildklierdiagnostiek, wat me nu bij MDO's beter in staat stelt om de gevolgen van bepaalde beleidskeuzes bij patiënten te beredeneren en vragen te stellen over de informatie die nodig is om de uiteindelijke keuze het best te onderbouwen.

2) **Zekerder en vaardiger worden in communicatie met patiënten en artsen op de (endocrinologie)poli, om gezamenlijk de benodigde informatie te achterhalen waarmee het beleid voor de patiënt onderbouwd kan worden.**

In de tweede helft van deze stage liep ik op de woensdagochtend mee op het schildkliерspreekuur van de endocrinologie. De eerste 3-4 keer liep ik alleen mee met de endocrinoloog om een beeld te krijgen welke specialistische informatie de endocrinoloog vooral wil weten van de patiënt. Op deze poli krijgen nieuwe patiënten eerst een algemeen gesprek met een doktersassistent en dan direct aansluitend het gesprek met de endocrinoloog. Ik ging daarna ook bij dit voorgesprek mee en mocht dat zelf gaan doen, waarbij ik het vertrouwen kreeg om zonder supervisie deze voorgesprekken te doen. Het doel van dit voorgesprek is om een beeld van de patiënt te krijgen door klachten uit te vragen, de speciële- en tractusanamnese (schildklier) te doen, en bloeddruk en gewicht te meten. De endocrinoloog hoeft dan alleen de anamnese aan te vullen waar nodig is en kan daarna vooral het (specialistische) beleid met de patiënt bespreken.

In het begin probeerde ik alle vragen die ik in het voorgesprek aan elke patiënt wilde stellen goed voor te bereiden en te onthouden, waarbij ik elke vraag evenveel prioriteit gaf, omdat ik nog niet echt kon inschatten wat meer of minder prioriteit had. In de praktijk lukte het niet om alle vragen evenveel aandacht te geven binnen het tijdsbestek van een poligesprek. Tegen het eind van elk poligesprek werd de kans groter dat ik mijn laatste vragen ging vergeten, afhankelijk ook van hoe een gesprek loopt en wat de patiënt zelf vertelt en vraagt. Doordat ik alle vragen perfect wil kunnen stellen, maar niet per se in volgorde van prioriteit, heeft dit bij vorige stages geleid tot onnodige onzekerheid. Ik wilde dit keer dan ook vooral de focus houden op de informatie met hoge prioriteit (en niet zozeer op hoe ik foutloos een poligesprek kan doen).

Voorafgaand aan de poli bereidde ik alle patiënten voor en probeerde ik de zaken/vragen met hogere prioriteit voorop te houden. Deze voorbereiding deed ik samen met de endocrinoloog of doktersassistent, waardoor ik kon toetsen of ik in de goede richting zat. Door dit elke woensdagochtend eerst te doen en daarna de poligesprekken zelf te oefenen, wilde ik vaardigheid ontwikkelen in de juiste prioriteiten stellen, wilde ik minder lang stilstaan bij elke stap die ik ga zetten en zekerder worden. Ik kreeg vanuit de kliniek de feedback dat ik heel prettig was in de omgang, goed was in kalm blijven, in rust bewaren, in uitleg geven aan de patiënt en duidelijk de informatie die ik uit de patiënt had verkregen kon overbrengen naar de arts. Het grootste verbeterpunt wat ik kreeg was dat ik nog steeds informatie van patiënt met hogere prioriteit kon vergeten voor informatie die minder relevant was. Als ik in een poligesprek de structuur kwijt ben en niet weet wat ik moet zeggen heb ik de neiging de eerste vraag die in me op komt te stellen, ook als die niet heel relevant is. Ik heb moeten leren om het niet erg te vinden de structuur in een poligesprek kwijt te raken en met hulp van de patiënt, collega's of patiëntgegevens uit de computer die weer terug te vinden. Waar ik eerder liever pas de patiënt sprak als ik alles perfect vooraf had uitgezocht (en ook pas de arts sprak bij het overdragen van klinische gegevens), merk ik nu dat ik het niet vervelend vind om uit te zoeken wat ik ben vergeten in de aanwezigheid van de patiënt of arts. Sterker nog, daar werd waardering voor uitgesproken. Ik voel me comfortabeler om ook tijdens een poligesprek zelf aan te geven dat ik iets niet weet en schrijf de vraag dan voor de arts op, om er later weer op terug te komen. Ik neig nu minder snel naar minder relevant dingen om ervoor te zorgen het gesprek op gang te houden, waardoor ik de informatie met hogere prioriteit de kans geef op de voorgrond te blijven.

3) **Met behulp van de richtlijnen leren onderbouwen of een patiënt wel/niet doorgestuurd moet worden in het traject van de schildklier(kanker)patiënt en wat daarin beperkingen nog zijn.**

Ik had me dankzij mijn opdracht en de MDO's verdiept in jodiumtherapie en refractaire ziekte. Deze verdieping betrof vooral het eindstadium van schildklierkanker. Ik wilde graag ook meer

weten van de stadia ervoor, omdat de behandelingen die daar gedaan worden blijvende impact hebben op de patiënt en ook op de overwegingen voor jodiumtherapie. Ik wilde zien wat de overwegingen zijn om de patiënt door te sturen naar het volgende stadium en welke ervaringen patiënten meenemen tot aan het eindstadium. Ik ben bij de endocrinologie meegelopen, zoals hierboven genoemd. Daarnaast ben ik met hoofdhals-chirurgen meegelopen om meer over de thyreoïdectomie en halsklierdissectie te leren. Ik mocht aan tafel assisteren, waardoor ik de uitdagingen bij het verwijderen van weefsels in de hals, waar belangrijke vaten en zenuwen in de buurt lopen (permanente beschadiging van de stembandzenuwen tijdens de operatie kan de levenskwaliteit en toekomstige behandelingen van een patiënt beïnvloeden), heb mogen ervaren. De gevolgen van de operatie hebben invloed op het vervolgtraject van de patiënt. Ook heb ik op het schildkliерspreekuur van de chirurgie meegelopen en geleerd hoe een dergelijke operatie met de patiënten wordt besproken, waar ik direct mijn kennis van de operatie mocht testen door vragen van de patiënt te beantwoorden en uitleg over de operatie te geven.

Ik heb hierdoor dezelfde patiënten langs zien komen bij de chirurgie, endocrinologie èn jodiumtherapie. Ondanks dat deze patiënten in hetzelfde traject zaten en onder dezelfde landelijke richtlijnen beoordeeld worden, was de (dosis) jodiumtherapie en de route daar naar toe verschillend. Dit kwam bijvoorbeeld doordat de tumor/positieve lymfeklieren soms niet geheel verwijderd konden worden. Ik heb deze 2-3 patiënten met de chirurg, endocrinoloog en nucleair geneeskundige kunnen bespreken en probeerde daarbij de landelijke richtlijnen van elk stadium toe te passen. In sommige situaties kunnen de richtlijnen (en sommige patiëntonderzoeken) tekort schieten, waardoor er onzekerheid is over wat de hoogste kans voor de patiënt kan geven op curatie en/of verbetering van levenskwaliteit. Een voorbeeld is bij een patiënt die een kleine schildkliertumor had, waarbij het volgens de richtlijnen nog te klein was voor een operatie. Ondertussen leek die tumor aan de hand van een biopt en echo buiten het schildklierweefsel te groeien, wat de noodzaak van verwijdering weer groter leek te maken. Een ander voorbeeld waar tegen aangelopen werd was dat zelfs na meerdere naaldbiopten uit een schildkliertumor niet definitief vastgesteld kon worden of de kans groot was dat de tumor kwaadaardig was/ging worden. Weer een voorbeeld was over hoe je zeker kan weten of de tweede helft van de schildklier eruit moet, als pathologische analyse van de verwijderde eerste helft geen duidelijk uitslag biedt. In dit soort lastige situaties lukte het mij in het begin niet om tot dezelfde overwegingen voor het vervolgtraject te komen als de artsen (wat ik kon toetsen aan de hand van de MDO's waar deze patiënten besproken werden). Na vaker oefenen tijdens het meelopen bij de verschillende stadia lukte het beter en kreeg ik te horen dat ik vragen met meer diepgang begon te stellen, die makkelijker leiden tot de juiste overwegingen.

Overige klinische activiteiten waren bijvoorbeeld meelopen bij werkzaamheden op de nucleaire geneeskunde. Deze activiteiten vielen buiten de schildklierthematiek en waren vooral bedoeld als verbreding naar andere casuïstiek binnen de nucleaire geneeskunde, om inzicht te krijgen in de rollen en om een connectie te bouwen/onderhouden met de afdeling. Zoals: zelf (SPECT/PET-)scans beoordelen en verslaan, meelopen bij de SPECT en de PET, inspanningstesten, botdichtheidsmetingen en poli. Bij het beoordelen van scans kreeg ik de feedback dat ik snel de essentie en (fysische/fysiologische) mechanismen van de scan goed begreep en als er ziekte te zien was, ook goed kon aangeven waar dat zat. Als verbeterpunten kreeg ik dat de informatie die ik uit een scan haalde nog incompleet en ongestructureerd was, waardoor ik nu meer let op het mezelf stellen van vragen over wat ik nog niet zie op de scan i.p.v. wat ik wel zie. Door te helpen bij de RESET studie heb ik geleerd met radioactief (patiënten)materiaal om te gaan en heb ik venapuncties gedaan bij patiënten die straling afgaven.

Persoonlijke Ontwikkeling

Ik heb snel de neiging in mijn eentje zonder hulp de antwoorden te willen vinden op vraagstukken en onduidelijkheden. Het voelt voor mij snel alsof ik iemand lastig val als ik vragen heb. Ook deel ik mijn gedachteproces pas liever als ik heel zeker van mijn zaak ben en vond ik het nooit prettig om het toe te geven als ik vast zat. Dit zat me nooit echt in de weg bij vakken en tentamens, waar ik goed genoeg kon studeren om voldoendes te halen. Echter begon het soms problemen te geven toen ik stages ging doen.

Als ik bij een stage vast zat wilde ik het zelf oplossen, dook ik de details in en communiceerde ik te weinig, waardoor ik de neiging had uit beeld te verdwijnen. De beslissing om toch naar begeleiders te stappen voor sturing kwam vaak (te) laat. Achteraf bleek dan dat het om een denkfout ging en dat een kleine suggestie van een begeleider genoeg zou zijn geweest om me weer in de goede richting te sturen. Ik kon soms meerdere kleine problemen laten opstapelen tot een complexer geheel en dan was het voor begeleiders lastig om nog last minute te helpen het op te lossen. Als ik feedback wilde vroeg ik dat meestal na het zetten van grote stappen, wat het lastig kon maken om mijn gedachteproces goed te laten zien. Daarbovenop heb ik überhaupt de neiging heel erg de details in te willen duiken bij het inlezen in een project, zonder eerst af te stemmen hoe het grotere plaatje eruit komt te zien. Dit kan tot onnodig werk en verlies van het overzicht leiden. Ik maak het hierdoor voor mezelf soms lastiger dan nodig is, wat ook tot onzekerheid heeft geleid.

Ik leerde uit vorige stages dat er niet meer van mij werd verwacht dat ik de juiste kennis bezit, en die laat zien op een paar momenten, zoals met tentamens. Als ik me wilde blijven ontwikkelen moest ik op meerdere momenten gaan laten zien welke kennis ik juist nog niet heb (met een plan hoe die kennis te verkrijgen). Dan kunnen anderen meedenken en beter inschatten wat voor soort hulp het meest voor mij kan betekenen. Met deze kennis wilde ik deze M3 stage proberen het makkelijker en efficiënter voor mezelf te maken door te oefenen met input van begeleiders vragen. Aan het begin van deze M3-stage heb ik een enquête gemaakt met vragen over hoe ik overkom op mensen, waarbij steeds een cijfer op een schaal van 1-10 gegeven moet worden. Dit waren vragen over hoe zeker, assertief, open en spontaan ik overkwam. Ik liet deze enquête 2 maanden lang elke week door 2-3 mensen invullen. Ik wilde hiermee aan de start van de stage meteen toetsen hoe mensen de omgang en samenwerking met mij ervaren en om feedback te krijgen over wat ik kan doen om een plek binnen een afdeling in te nemen op een manier die voor iedereen werkt. De resultaten van de enquêtes waren positief. Mensen vonden mij op een schaal van 1-10 vaak een 7 of hoger op de meeste thema's. Alleen op assertiviteit is wel eens een 4 ingevuld. Met de zelfkennis die ik naar deze M3 had meegenomen en met de resultaten van de enquête had ik persoonlijke leerdoelen opgesteld.

Ik wilde deze stage duidelijkheid voor mezelf en begeleiders creëren als ik merkte dat ik iets niet helemaal begreep.

Ik ben deze stage vaker uit mijn comfortzone gestapt door laagdrempelige vragen te stellen over wat ik nog niet begreep. Ik heb bij de voorbereiding van de wekelijkse contactmomenten met begeleiders aandacht gegeven aan de kern en het overzicht van wat er moest gebeuren. Elke dag schreef ik aan het begin maximaal 3 taken op die moesten gebeuren (is 80% van de dagen gelukt), om niet te veel tegelijk te doen en stap voor stap te werken. Dit heeft voorkomen dat ik vast kwam te zitten in details die bijzaak zijn en dat ik bleef zwemmen. Ik ben beter geworden in het herkennen wanneer ik te lang aan het zwemmen ben en heb begeleiders vaker om hulp gevraagd. Bij het krijgen van feedback over mijn werk maakte ik meteen notities en heb ik vaker om verheldering gevraagd voor extra duidelijkheid voor mezelf. Ook ben ik meer tussendoor gaan

verifiëren of ik op het goede spoor zat door even kort iets te laten zien of te vragen. Dat laatste deed ik met name met mijn dagelijkse begeleider. Hierdoor heb ik onnodig werk voorkomen en heb ik mijn inspanningen veel efficiënter gebruikt om te werken richting een doel waar begeleiders meer betrokken bij waren. Ik heb geleerd dat met hulp en bevestiging vragen je het makkelijker en efficiënter voor jezelf kan maken.

Ik ben niet de persoon die het snelst op iemand afstapt en geef daardoor mensen niet altijd de kans om mee te denken. Dat kwam ook uit de 360 graden feedback naar voren en dit is nog steeds een persoonlijk thema voor mij, bij een toekomstige baan. Deze valkuil zal blijven bestaan, maar ik heb geleerd hoe ik met gerichte input van anderen er snel weer uit kan komen en dat het niet erg is om met hulp uit een valkuil te moeten stappen. Ik heb deze stage plezier beleefd aan het samenwerken en samen zoeken naar oplossingen van problemen, waar ik me gewaardeerd voelde om mijn inbreng en manier van werken. Ik werd onderdeel van een team wat samen aan een project werkt in plaats van een student die een cijfer moet krijgen. Dit heeft zekerheid in mezelf opgeleverd en heeft me doen inzien dat ik een TG'er ben die goed is in informatie absorberen en uitleg geven. Ik kan alleen soms te lang in de theorie blijven hangen. Daar biedt samenwerking met mensen die snel naar de praktijk overstappen uitkomst in.

Ik wilde bij tegenslagen sneller tot actie komen en het daarna achter me laten

Ik wilde ook beter leren omgaan met onzekerheid en tegenslagen. Ik voelde onzekerheid over het maken van fouten en krijgen van kritische feedback, waardoor ik afwachtend ben. Door te lang af te wachten na een tegenslag duurt het lang voordat er weer iets gebeurt en blijf ik het onnodig lang bij me dragen. Ik wilde deze stage niet de nadruk leggen op die onzekerheid en de focus leggen op waar ik de meeste plezier kon vinden tijdens de stage. Voor mij zit dat plezier vooral in het proces van samenwerken. Deze stage heb ik met artsen, TG'ers, laboranten en klinisch fysici kunnen samenwerken en brainstormen over alle experimenten die ik voor mijn opdracht heb gedaan. Ik reken tegenslagen mezelf vaak zwaar aan. Ik had bijvoorbeeld een keer een miscommunicatie waardoor ik de resultaten uit die metingen verkeerd had geïnterpreteerd, waarna ik niet goed wist hoe ik het moest oplossen. Door dit aan te geven (ook aan de rest van de begeleiders) en om uitleg te vragen werd het me duidelijker wat de juiste interpretatie was en werd het probleem daardoor een stuk kleiner.

Het liefst wil ik tegenslagen voorkomen, wat ik heb geprobeerd door regelmatig (minstens elke twee weken op vaste meetings) te verifiëren bij al mijn begeleiders of ik op het goede spoor zat. Als ik veel feedback of kritische vragen kreeg waarop ik het antwoord niet wist, gaf ik dit aan. Hierbij verwerkte ik de feedback eerst zelf, maar probeerde ik niet langer dan een dag er in te blijven hangen. Als ik er dan nog niet uitkwam, vroeg ik of begeleiders weer wilden meedenken. Als ik onduidelijkheid ervaarde heb ik de neiging hele specifieke vragen over details te stellen, wat afleidend kan zijn en iemand anders minder goed de kans geeft om erachter te komen wat ik niet snap. Tijdens deze stage pakte ik het anders aan en gaf ik bij onduidelijkheid aan wat mijn interpretatie was en of anderen wilden meedenken. Hierdoor kwam (kritische) feedback meestal niet als een verrassing, omdat we dezelfde punten (die ik moeilijk vond) steeds beter identificeerden en bespraken. Door deze hulp, duidelijkheid en communicatie heb ik tegenslagen sneller en efficiënter achter me kunnen laten en zijn de negatieve associaties bij het maken van fouten kleiner geworden. Ik heb geleerd dat fouten maken onvermijdelijk is en dat hiermee omgaan belangrijker is dan alles proberen in één keer goed te doen. Een tegenslag krijgen zegt niks over wat je wel of niet kan en leidt uiteindelijk tot verbetering. Ik kan na deze stage de gevolgen van iets fout doen beter leren relativeren.

Ik wilde de theorie efficiënter omzetten tot behapbare actiepunten in een duidelijke planning

Ik heb vanaf het begin van deze stage met mijn begeleiders gecommuniceerd over wat voor persoonlijkheid ik ben en wat mijn handleiding is (o.a. met dank aan de enquête). Daardoor konden zij vanaf dag één meedenken en kreeg ik vrij snel de feedback om niet te lang in details te blijven hangen. Om niet te veel te zwemmen en om op één lijn te blijven met de begeleiders, wilde ik dat zij op de hoogte zouden blijven van waar ik mijn energie in aan het steken was. De energie die ik normaal misschien meer in het onderzoeken van details zou steken, ging ik nu meer steken in het bedenken van overzichtelijke stappen, die ik in tijdsperiodes van 1 tot 2 weken steeds kon zetten. Deze stappen presenteerde ik elke 2 weken op ons vast overleg en zo kon ik makkelijk laten zien met welke stappen ik nog bezig was en welke stappen er in de toekomst aan kwamen. Hierdoor was er duidelijkheid, maakte ik het makkelijker voor mezelf door mijn stappen meteen te laten toetsen naar haalbaarheid en had ik er plezier in. Hierdoor kreeg ik meer vertrouwen in wat ik aan het doen was.

Uitstellen Afstuderen

Ik wilde initieel op 25 augustus afstuderen, maar het lukte niet om op tijd een volwaardig conceptverslag met feedback af te hebben voor die datum. Ik leverde in juli alles wat ik had in. Er was daarna nog veel werk nodig aan Part II van het verslag, zeker in vergelijking met Part I. Op de general discussion was er ook veel feedback, meer dan ik had verwacht. Ik dacht dat ik de belangrijkste implicaties van mijn resultaten op een rij had in de general discussion, maar na de feedback begreep ik dat het warrig was opgeschreven en dat discussie over toekomstperspectieven nog ontbrak. Dit was teleurstellend na een maand schrijven, maar na het lezen van de feedback begreep ik duidelijk wat er nog ontbrak. De resultaten van Part II en stukken discussie uit alle delen van het verslag waren nog te weinig samen besproken en daardoor nog onvolledig, iets wat bij Part I wel beter ging. Dat het bij Part I goed ging komt door het landelijke symposium waar ik Part I heb gepresenteerd. Door die stok achter de deur lukte het beter om overzicht te houden en voelde het natuurlijker om alles gezamenlijk door te bespreken.

Na advies van begeleiders, collega's, familie etc. te hebben gevraagd leek mij het niet verstandig om het M3 af te raffelen en koos ik voor een No GO voor 25 augustus. Ik vond het niet de makkelijkste keuze, vooral omdat het lastig inschatten was hoe lang ik nodig zou hebben om een beter conceptverslag te maken, waarmee afstuderen op 25 augustus eventueel nog haalbaar had kunnen zijn. We spraken meteen een nieuwe afstudeerdatum af. Iedereen kon pas op 20 oktober wat extra tijd gaf. We besloten van deze extra tijd gebruik te maken door elke week een stukje van het verslag te herschrijven en te laten voorzien van feedback. Voor Part II werkte dit vrij goed naar mijn idee, waardoor ik meteen een grote slag kon maken. Met de general discussie vond ik het lastiger en merkte ik dat er meer bijgestuurd moest worden. De discussie vereist dat je een goed overzicht hebt van je resultaten, maar ook over wat je nog nodig hebt voor toekomstig onderzoek. Met een dergelijk groot (M3) project vond ik het lastig om het overzicht paraat te hebben en tussendoor ook in elk onderdeel weer de diepte in te duiken.

Ik trok hier wederom de les uit dat het waardevol is om op tijd je progressie en interpretatie van je voortgang te delen, zodat anderen de kans hebben om met inzicht en suggesties te komen die je zelf misschien niet snel bedenkt. Daardoor had met bijsturing voorkomen worden dat het plan nog zo laat moest worden omgegooid. Toen duidelijk werd verslag aangepast moest worden, moest er dus ook snel een plan komen wat ik met de afstudeercommissie moest afstemmen. De begeleiders communiceerden om niet te lang stil te blijven staan in hoe het tot dat punt gelopen

was en vooral door te gaan met het maken van een nieuw plan. Door de hulp en deze communicatie van de begeleiders had ik de aanmoediging die ik nodig had om met hen samen een nieuw plan te maken. Het uitstellen van het afstuderen voelde daardoor niet als een tegenslag. Er was achteraf dus wat meer tijd nodig om alle implicaties van mijn onderzoek dit jaar beter te begrijpen en op te schrijven. Dat was niet erg. De les was om regelmatiger mijn interpretatie van de resultaten en discussie te delen, zodat noodzakelijke wijzigen in de planning minder vaak en minder onverwacht gebeuren.

Ontwikkeling tot Professional

De uitdagingen die ik tegenkwam bij het ontwikkelen tot een professional in het werkveld wil ik illustreren door gebruik te maken van de 6 competenties van het TG beroep.

Technisch-medisch deskundige

Ik ben goed in theorie leren en in dit goed overbrengen. Ik kan veel tijd steken in het opnemen van kennis, maar heb ook ervaren dat je niet altijd tijd hebt om je optimaal voor te bereiden en dat het dan belangrijk is om in de gaten houden wat je nog moet weten om iets te betekenen voor een collega en/of patiënt. In situaties waar ik denk niet voldoende te weten kan ik makkelijk stil worden en naar de achtergrond treden, uit een irrationele angst om door de mand te vallen. Dit zijn juist situaties waar je jezelf kan verrijken met nieuwe kennis, door goed te communiceren wat je graag wilt weten. Anders verwoord: Ik sta open voor situaties waarin ik mijn kennis kan laten zien, maar dus minder voor situaties waar anderen hun kennis kunnen laten zien. Ik heb dit jaar geprobeerd zoveel mogelijk te halen uit situaties waar ik eigenlijk voelde niet genoeg kennis te hebben om mee te kunnen praten. Een voorbeeld is op de OK bij de thyreoïdectomieën waar ik weinig wist over hoe de chirurgen precies te werk gaan. Normaal zou ik dan liever niet een te grote afleiding willen vormen. Ik heb dit keer juist vragen gesteld over wat ik zag, wat ze aan het doen waren en waarom. Ik merkte daardoor dat de chirurgen graag wilden antwoorden, uit zichzelf erover begonnen te vertellen en enthousiast werden. Van 'door de mand vallen' was geen sprake. Ik heb uit deze ervaringen dit jaar kunnen halen dat, afhankelijk van de situatie, het in een werkomgeving niet vanzelfsprekend is om altijd de juiste kennis paraat te hebben. Daar kun je professioneel mee omgaan, door goed te laten weten waar je qua kennis staat en aan te geven wat je wil weten/leren.

Communicator

Bij onzekerheid vind ik het lastig om te communiceren. Ik ben goed in de rust en kalmte bewaren in een gesprek en kies mijn woorden voorzichtig. Maar soms geef ik de manier van communiceren prioriteit boven het behalen van het doel van de communicatie. Ook kan ik te makkelijk denken dat ik een onzekerheid alleen kan oplossen, waardoor ik stil val en het niet duidelijk is voor de omgeving wat ik probeer op te lossen. Ik wil ook tegengas kunnen geven en mijn grenzen kunnen aangeven als nodig. Ik wilde mijn communiceren deze stage meer op het doel focussen dan op de manier van communicatie zelf. Om het doel te halen heb ik input nodig van anderen en moet ik het kunnen aangeven als ik denk dat mijn koers niet gelijkt loopt met de koers van anderen. Ik heb deze stage moeten samenwerken met klinisch fysici, laboranten en verpleging om mijn metingen te organiseren. Hierbij heb ik aangegeven wat voor hulp ik nodig had en had ik goed contact met iedereen. Iedereen met wie ik heb gecommuniceerd deze stage was enthousiast, en wilde hulp aanbieden en sparren als ik uitleg gaf over wat ik deed en wat ik nog wilde weten. Ik denk dat de communicatie goed ging deze stage, maar dat er ook nog winst te behalen valt. Zo was het bijvoorbeeld voor iemand die niet bij mijn overleg aanwezig kon zijn, naderhand niet altijd duidelijk wat er besproken was. Ik vond het lastig overzicht te houden over wie van wat op de hoogte was en had het mezelf makkelijker kunnen maken door mijn communicatie op een grotere groep

betrokkenen te richten (via cc). Ik wilde nog te vaak mijn communicatie afstemmen op het individu en per persoon contact te zoeken (uit een soort beleefdheid).

Samenwerker
Ik kon deze stage niet volbrengen zonder samen te werken met mijn begeleiders en collega's. Ik heb de neiging op alle aspecten graag te willen bewijzen dat ik het zonder hulp zou kunnen, wat ook bijdraagt aan dat ik het doel en overzicht uit het zicht kan verliezen. Echter vond ik het op deze stage heel fijn om niet overal het onderste uit de kan te halen en maakte ik gebruik van de input van anderen. Ik heb geleerd dat alle rollen in het ziekenhuis, ook die van de TG'er, afhankelijk zijn van elkaar. Ik heb gezien dat als je aangeeft wat je wil, iedereen zeer bereid is om mee te denken. Als TG'er probeer je dingen die minder bekend zijn te implementeren en dat betekent dat de hulp die anderen kunnen geven daar misschien op afgestemd moet worden. Bij de uitvoering van een aantal metingen met SPECT had ik bijvoorbeeld de expertise nodig van laboranten om de juiste instellingen te gebruiken. Zij hielpen met alles klaarzetten voor onze metingen, maar ze wisten in eerste instantie niet precies waar onze metingen voor bedoeld waren. Voor een goede samenwerking moet je als je hulp vraagt duidelijk aangeven wat voor hulp je precies wil. Als iemand om jouw hulp vraagt moet je duidelijk aangeven wat voor hulp je precies kan bieden. Anders zul je snel langs elkaar gaan werken. In een professionele omgeving is het cruciaal om snel van elkaar te weten wat je aan elkaar hebt en dit neem ik na deze stage met me mee.

Organisator
Ik heb deze stage mijn organisatie-skills moeten gebruiken om kliniek, SPECT/PET metingen en overleggen te organiseren. Ik ben goed in afspraken voorbereiden, waardoor het meestal wel lukte om input te krijgen en weer stappen verder te zetten. Ik heb de neiging om soms graag te voorbereid te willen zijn, waardoor ik in de voorbereiding blijf hangen en niet doorpak, ook niet als de tijd krap is. Ook als het overbodig lijkt wil ik nog steeds graag alles afwegen voordat ik actie onderneem en dan stel ik me er op in dat het weken gaat duren voordat alles lukt. Ik ben me er bewust van dat in deze omgeving anderen niet altijd tijd voor je hebben en dat niet iedereen kan wachten tot ik mijn lange voorbereiding af heb. Ik voel me soms tegengehouden om dingen snel op korte termijn te regelen, omdat ik me dan onvoorbereid vind en er al vanuit ga dat het niet gaat lukken. Vaak is er juist veel mogelijk op korte termijn, maar daar kom je niet achter als je het niet probeert. En als het toch mislukt is het ook niet erg, omdat je er nog op tijd bij bent. Deze stage wilde ik minder lang vast zitten in bijzaken en sneller stappen richting een doel communiceren/ondernemen. Dit ging vaak goed. Uiteindelijk is de bulk van mijn metingen en van mijn kliniek steeds binnen een dag georganiseerd. Hierdoor kwam ik enthousiast over, waardoor ook het enthousiasme bij chirurgen en endocrinologen groeide en ik uitgenodigd werd om wekelijks mee te lopen.

Academicus
Ik wil een goede basis beheersen als het aankomt op academische vaardigheden. Ik ben goed in teksten analyseren en in presenteren, maar vind het soms lastig om te bedenken wat ik met (mijn eigen) data moet doen. In de literatuur heb ik voorbeelden gezien waar de grote kern duidelijk in de introductie, methode, resultaten en discussie steeds naar voren komt. Hierdoor heb ik geleerd dat bij een goed afgebakende onderzoeksvraag, er een logische methode uit moet kunnen vloeien. Dit overzicht behouden is een belangrijk aspect dat van een TG'er verwacht mag worden. Details die erbij komen moeten naar de achtergrond treden op het moment dat ze niet relevant zijn of als het overzicht verloren dreigt te gaan. De data die ik heb verzameld in deze stage vereisten geen complexe statistiek, maar elke soort meting had een net wat andere manier van uitwerken nodig.

Ik denk dat ik mezelf helemaal had kunnen verliezen in details als ik complexere statistische methoden had moeten uitzoeken. Gezien mijn valkuilen was het goed dat ik nu kon oefenen met data waarbij het overzicht, consistentie binnen metingen en reden van uitvoering belangrijk waren. Het is gelukt om de overzicht te behouden, waardoor de resultaten duidelijk waren te volgen voor begeleiders en er gerichter feedback op gegeven kon worden. Ik hoop dat vast te kunnen houden voor de toekomst.

Ik vond het interessant om op de hoogte te blijven van het andere onderzoek wat op de afdeling plaats vond, maar vond het soms lastig het jargon of onderzoeksmethoden die ik nog nooit had gebruikt te begrijpen. Ik heb de onderzoekers om uitleg gevraagd en ik heb ook literatuur gelezen over mijn eigen onderwerp, waar ook verschillende onderzoeksmethoden gebruikt worden. Naast het opdoen van meer kennis en ervaring over wetenschappelijk onderzoek, heeft dit ook geholpen het overzicht te houden bij mijn eigen stageopdracht. De medeonderzoekers hebben mij 3 keer mijn onderwerp zien presenteren en ik kreeg daar complimenten over.

Beroepsbeoefenaar/Professional

Ik ben deze stage bezig geweest met wat ik lastig vind (overzicht houden, hulp vragen, gedachteproces delen en doorpakken) en tot welke gevolgen dat kan leiden bij het beoefenen van dit beroep. De worst-case scenario is dat ik bij toegenomen druk, bijv. door tijdgebrek na een te lange voorbereidingsfase, een actie onderneem uit een te snelle conclusie die met een denkfout is getrokken. Waarna, ondanks goedbedoelde intenties, de actie verkeerd uitpakt of collega's onaangenaam verrast. Een denkfout is lastig om in je eentje te ontdekken en kan vaak alleen door een ander eruit worden gepikt, maar pas als je je resultaten en conclusies regelmatig deelt. Ik besef me dat het niet erg is om denkfouten te maken, maar wel om ermee te blijven zitten. Ik wil een TG'er worden die rekening kan houden met denkfouten bij zichzelf en anderen. Voorafgaand aan belangrijke evenementen/presentaties wil ik er voortaan op tijd bij zijn met het bespreken van mijn resultaten en conclusies, ook al zitten er dan misschien nog grote (denk)fouten in. Dat is deze stage deels goed gegaan. Bij ons vast overleg zijn met name de SPECT-resultaten besproken. Ook omdat ik deze resultaten op het symposium van de NVNG wilde presenteren, waardoor er vroegtijdig 2-3 revisies zijn geweest van dit stuk. Hierdoor had ik ook vertrouwen in dat de presentatie op het symposium goed zou gaan en dat ging het ook. Het PET-onderdeel is minder besproken en ik merkte daar dus ook minder zelfvertrouwen in.

Ik ervaar vaak een drempel als ik ergens niet zeker van ben. Die drempel lijkt te bestaan uit interne factoren (niet tot last willen zijn en denken dat ik het alleen moet kunnen oplossen) en externe factoren (laagdrempelige omgeving en externe aanmoediging). In deze stage kreeg ik de feedback van de begeleiders om de hele opdracht te zien als een teameffort en dat heeft mij aangemoedigd om vaker de drempel te nemen.

Ik ben ook bezig geweest met wat mijn krachten zijn (theorie begrijpen, analyseren, presenteren, snel leren, uit meerdere perspectieven kunnen kijken, prettige sfeer creëren en uitleg geven). Ik heb klinisch en qua onderzoek veel uit deze stage kunnen halen, meer dan ik vooraf had verwacht. Ik ben ook blij dat hoewel de opdracht zelf vrij technisch van aard was, mijn activiteiten in de kliniek er toch mooi op aansloten. Tot slot ging de samenwerking met andere collega's goed, wat leidde tot uitnodigingen om vaker langs te komen en tot meedenken over mijn opdracht. In een toekomstige baan wil ik van deze krachten gebruik maken, ook om de lastige drempels te verlagen.

Afsluitend

Voor mij was dit een jaar waar ik vooral terugdenk aan de gezellige tijd die ik hier heb gehad en aan de vele activiteiten die na werk gezamenlijk ondernomen werden. Ik heb altijd het gevoel gehad dat alles openlijk besproken kon worden, wat voor een hele prettige sfeer zorgde. Ik ben mijn begeleiders dankbaar dat ze me hebben geholpen en me hebben uitgedaagd om altijd een stap verder te denken. De afdeling bevat een grote diversiteit aan persoonlijkheden met wie ik veel heb kunnen lachen en van wie ik heb geleerd dat er meerdere manieren mogelijk zijn om tot een doel te komen.

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