GUIDELINES FOR POSITIONING, IMMOBILISATION AND POSITION VERIFICATION OF HEAD AND NECK PATIENTS FOR RTTs

Edited by:
Michelle Leech

Michelle Leech

Mary Coffey
Mirjam Mast
Filipe Moura
Andreas Osztavics
Danilo Pasini
Aude Vaandering

Acknowledgements

The authors would like to extend our thanks to the following for their contribution to these guidelines:

Ms. Suzanne van Beek MSc., Mr. Stephen Coyne, Mr. Jaap Kuipers, Mr. Ruud Wigggenraad MD, Mr. Jan van Santvoort and Mr. Paul Bijdekerke for sharing vignettes of their current practice.

Mr. Velimir Karadza and Ms. Tatiana Petrova for their assistance in translating the survey.

Dr. Ricardo Seguardo for his assistance with statistical analysis.

Ms. Chiara Gasparatto from the ESTRO office for her kind assistance.

Michelle Leech
December 2016

Contents

List of Tables

List of Figures

List of Abbreviations

3DCRT	3-Dimensional Conformal Radiation Therapy
AP	Anterior-Posterior
CBCT	Cone Beam CT
CC	Cranial-Caudal
CT	Computed Tomography
CTDI	Computed Tomography Dose Index
CTV	Clinical Target Volume
DLP	Dose Length Product
DRR	Digital Reconstructed Radiograph
e-NAL	Extended no action level
EPI	Electronic Portal Image
EPID	Electronic portal imaging device
FOV	Field of View
GTV	Gross Tumour Volume
Gy	Gray
IMRT	Intensity Modulated Radiation Therapy
IV	Intravenous
kV	Kilovoltage
MRI	Magnetic Resonance Imaging
NAL	No action level
NTCP	Normal Tissue Complication Probability
OBI	On-board imaging
PRV	Planning Organ at Risk Volume
PTV	Planning Target Volume
RO	Radiation Oncologist
RT	Radiation Therapy
RTT	Radiation TherapisT
SAL	Shrinking Action Level
SIB	Simultaneous integrated boost
TCP	Tumour Control Probability
VMAT	Volumetric Modulated Arc Therapy
VOI	Volume of Interest
VS	Virtual Simulation

CHAPTER 1: INTRODUCTION

These guidelines have been developed to assist Radiation TherapisTs (RTTs) in positioning, immobilisation, position verification and treatment for head and neck cancer patients presenting for radiation therapy.

The document outlines the management of head and neck cancers and likely anticipated toxicities as well as reporting on current practice throughout Europe, both from a European survey and specific vignettes from RTTs across Europe. This practice is then discussed in accordance with the literature. Finally, a series of guidelines, based on the evidence are given, with a view to assisting RTTs in critical analysis of their own practice in relation to the positioning, immobilisation, position verification and treatment practices in their own centres.

1.1 Management of Head and Neck Cancers

Over the last decade, the management of locally advanced head and neck cancers (HNCs) has seen a substantial increase in the use of chemoradiation to improve survival rates and increase organ preservation. Cisplatin is now regarded as a standard chemotherapy agent and in combination with radiotherapy and the use of biological therapies, targeting both angiogenic and growth factor pathways, is becoming increasingly accepted as routine practice (1). However, these gains have seen a parallel increase in the frequency and intensity of toxicities, such as xerostomia, dysphagia, dysgeusia, speech difficulties and trismus. The impact of these toxicities on patient function and therefore quality of life has been well documented (2-6).

Minimisation of these toxicities is achieved through careful beam orientation and geometry selection as well as the innovative use of wedging and weighting when such patients are treated with a 3D Conformal (3DCRT) approach. In recent years, advanced techniques such as Intensity Modulated Radiotherapy (IMRT), Helical Tomotherapy and Volumetric Modulated Arc Therapy (VMAT) have been used with the view to minimising toxicities while maximising tumour dose. To achieve the aim of radiation therapy, HNC patients must be positioned and immobilised in a reproducible manner for all fractions. Position verification methods must also consider the dosimetric impact of shrinking tumour volumes and change in patient contour due to weight loss on dose to both the target volumes and to organs at risk (OAR).

Radiation TherapisTs (RTTs) must be aware of the impact of breaching dose volume constraints of OARs due to poor positioning and immobilisation or position verification procedures resulting in even greater significant acute and late toxicities for the HNC patients than would normally be expected.

1.2 Toxicities associated with chemoradiation for Head and Neck Cancers

In order to understand the importance of accurate positioning, immobilisation, position verification and execution of treatment, RTTs should be cognisant of the likely associated acute and late toxicities associated with the delivery of radiation therapy to the head and neck region. At treatment planning, RTTs, physicists, dosimetrists and radiation oncologists carefully ensure that specific dose volume constraints for OARs, such as those given by the Quantative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) (7) are adhered to, in order to reduce the likelihood of such toxicity and hence minimise the impact on quality of life (QoL). Similarly, adequate target volume coverage as given in the ICRU reports is also strictly adhered to. It is therefore incumbent on RTTs to carefully select the optimal patient position and immobilisation method both at CT scanning and on-treatment, as well as ensuring that the patient position is accurately reproduced over the course of fractionated radiation therapy. Failure to achieve this could result in breach of OAR constraints as well under dosage of target volumes, ultimately impacting on both TCP and NTCP.

1.2.1 Xerostomia

Saliva plays a major role in the maintenance of dentition, dilution of food detritus and bacteria and mechanical cleansing of the oral cavity. It also prevents oral infections and has other important functions including taste perception, formation of food bolus, facilitation of mastication, swallowing and speech as well as lubrication of the mucosa of the oropharynx and oesophagus. The parotid, submandibular and sublingual glands account for 90% of whole saliva production, with the minor salivary glands contributing the remaining 10%. Under resting conditions, about two-thirds of saliva is produced by the submandibular glands, which produce a mucin-rich fluid. The minor salivary glands, although only producing 10% of the total saliva contribution have a significant role to play in lubrication of the mucosa. Because of its many functions, patients with salivary gland hypofunction are usually restricted in their daily activities, have a poorer general well-being and can have limited social interactions (8).

Xerostomia was defined in a review by Jensen et al (6) as 'the subjective feeling of dry mouth', whereas salivary hypofunction was 'the objective measure of decreased salivary secretion'. Bhide et al (9) have found that patient-reported xerostomia scores achieve a correlation to absolute salivary flow rates, unlike physician-reported grading of xerostomia.

Patients with xerostomia often complain of a dry and sticky sensation in the mouth, which causes them considerable difficulty to chew dry food. They may also present with a decrease in taste sensation and discomfort wearing dentures. A decrease in saliva production can result in cracked lips, dry tongue, mouth sores and periodontal disease. According to dental literature (10), 'radiation caries' are a rapidly developing and highly destructive form of tooth decay after RT of malignant tumours in the head and neck region. Hyposalivation, induced by irradiation and dietary changes coupled with concomitant alteration of the oral flora, such as the

loss of bactericidal properties of saliva, encourages the growth of microbes such as streptococcus mutans, lactobacillus and candida species. These are considered to be the most important aetiological factors and hence remineralisation effects may be less likely in irradiated patients as the pH of any remaining saliva is too low. Bhide et al (9) report how all of these physical difficulties may ultimately lead to reduced nutritional intake and weight loss. In addition, xerostomia may contribute to the development of mandibular osteoradionecrosis after radiation.

Physical examination of the oral cavity in irradiated patients generally reveals a dry and sticky mucosa whose moist appearance is replaced with a thin and pale looking mucosa. Evidence of gingivitis may be seen and the pool of saliva normally seen in the floor of mouth is often absent. Management of such patients is complex. Visvanathan et al (11) divide the management of xerostomia into four categories:

1 General/Supportive measures which recommend:

- A daily fluid intake of minimum 2 litres per day
- Frequent sips of water
- Increased fluid intake while eating
- Avoidance of irritants such as smoking, alcohol and caffeine.
- Appropriate management of anxiety and stress

2 Salivary Replacements:

- Preparations are available as lozenges, sprays or gels and are either mucin or methycellulose-based, the former being better tolerated and having a longer duration of action.

3 Salivary Stimulants:

- Sugar free chewing gum enhances salivary flow by stimulating taste receptors.
- Pilocarpine is a muscarinic agonist which may take up to 12 weeks to take effect in radiotherapy-induced xerostomia. The increase in saliva production usually lasts for 4 hours. However its associated side-effects include perspiration, flushing, lacrimation and gastrointestinal disturbances. As a result of its cholinergic effect, it is contraindicated in patients with asthma, Chronic Obstructive Airways Disease (COAD), heart diseases, epilepsy, hyperthyroidism and Parkinson's disease.

4 Radioprotectants:

- Cytoprotective agents such as amifostine may minimise tissue damage secondary to radiotherapy and thereby decrease the incidence of radiation-induced xerostomia. The mechanism of action of these agents includes free radical scavenging, DNA protection and induction of hypoxia in tumour tissue. The American Society of Clinical Oncology (12) recommends that amifostine be considered in fractionated RT alone, but not in those treated with concurrent platinum-based chemotherapy as it is ineffective.

1.2.2 Dysphagia

Swallowing is a complex process and consists of voluntary and involuntary stages coordinated by both musculature and several cranial nerves (13). Levendag et al (14) outlines five musculature structures important in the swallowing process, namely the superior constrictor muscle (SCM), the middle constrictor muscle (MCM), the inferior constrictor muscle (ICM), cricopharyngeus muscle and the first centimetre of the muscular compartment of the oesophageal inlet. Dysphagia has been defined by Leslie et al (15) as: 'difficulty in swallowing which can be due to changes affecting any structure from the lips to the gastric cardia'. Many methods of quantifying dysphagia currently exist, from instrumental assessments such as videofluoroscopy (VF) where the oral, pharyngeal and oesophageal phases of swallowing can be visualised and fibreoptic endoscopic evaluation of swallowing (FEES) to patient-reported methods such as the M.D. Anderson Dysphagia Inventory (MDADI) and the observer-assessed subjective evaluations, such as the Common Terminology Criteria for Adverse Events (CTCAE) v.4.02.

Dysphagia causes not only functional impairment to the patient, but can impact on the normal activities of daily life. Roe et al (16) highlight the potential serious consequences of aspiration-related pneumonia and poor nutritional status in patients who may be immuno-compromised following treatment for head and neck cancer.

Preventative measures for swallowing problems reported in the literature include pre and post treatment exercises and the use of mechanical aids such as the Therabite (17,18). Caglar et al (19) also emphasises the use of swallowing exercises and interventions by speech and swallowing therapists on restoring swallowing function.

1.2.3 Dysgeusia

Dysgeusia can be defined as an impaired or abnormal sense of taste and usually refers to unpleasant tastes, which may be salty, bitter or metallic. It is possible that radiation therapy (RT) may alter the structure of taste pores or cause thinning of the papilla epithelium (20). Hong et al (21) have also described how compromised oral hygiene, postnasal drip, mucositis and infection can impact on dysgeusia in HNC patients. A systematic review of 14 studies by Hovan et al (20), reported a weighted prevalence of dysgeusia in a patient group receiving chemotherapy only as 56.3%, and 66.5% in a RT only group and increasing to 76% in a group receiving both chemotherapy and RT. This would indicate that chemotherapy may also cause damage to sensory receptor cells. While RT has a greater impact on dysgeusia than chemotherapy when administered in isolation, a combination of the two has a synergistic effect.

This review also found that up to 15% of patients treated with RT continued to experience dysgeusia post-treatment. However, the mean duration is not given, although there have been reports of incidences of dysgeusia up to 7 years post-RT (22). Treatment of dysgeusia is complex, with neither zinc supplementation nor amifostine demonstrating any proven benefit (23,24).

1.2.4 Trismus

Trismus is a tonic contraction of the muscles of mastication and limits the ability to open the mouth, which can lead to many associated difficulties for patients. These include poor oral hygiene, speech impairment and reduced nutritional intake due to compromised mastication ability (25). Bensadoun et al (26) report that trismus caused by RT may begin at any time towards the end of treatment or at any time during the following 2 years. The ability to open the mouth may become progressively worse over weeks or months.

CHAPTER 2: METHODOLOGY

2.1 Literature Review

A critical review of the literature was undertaken by the authors, searching relevant databases including PubMed, Embase and Google Scholar. Search terms used included combinations of 'head and neck cancer', 'radiation therapy', 'radiotherapy', 'positioning','immobilisation', 'verification', 'cone beam CT', and 'electronic portal imaging'. Studies in English, French, Portuguese, Italian and German were included.

2.2 Survey development and distribution

Based on the literature review, a survey was developed to ascertain the current positioning, immobilisation and position verification methods for head and neck radiation therapy across Europe. The survey consisted of 40 questions, divided into 5 sections. The sections contained both open and closed questions on: Demographics, Patient Positioning, Immobilisation devices, CT/Simulation Practice, Position Verification as well as elements of QA in relation to positioning and immobilisation.

The survey was piloted on 5 RTTs whose first language was English and the suggested minor phrasing changes were implemented. The survey was then translated into the following languages: Italian, Greek, German, Portuguese, Russian, Croatian, French and Spanish. All surveys, together with instructions, were subsequently uploaded into an online survey distributor, SurveyMonkey.

Contact details for RTTs in each European country were acquired through the ESTRO membership database as well as through the National Societies. An invitation email, both outlining its purpose and providing a link to the survey was sent to these contact persons in their own language, where possible. The contact RTT was asked to distribute the link to all departments nationally. In many cases, the survey was made available on National Society websites.

2.3 Data Analysis

Data analysis was performed using SPSS Statistics version 20.0 (IBM SPSS Statistics for Windows. Armonk, NY: IBM Corp.). Descriptive statistics were calculated and appropriate figures and tables constructed. Cross tabulations were performed where appropriate to maximise data analysis.

2.4 Vignettes of Practice

To further expand on the current practice across Europe, a number of RTTs were asked to provide a vignette of their departmental practice. For comparability purposes, RTTs were asked specifically to describe the practice in their departments

for locally advanced oropharyngeal patients undergoing definitive chemoradiation, as this was deemed to be a site commonly observed in the majority of radiation therapy departments where head and neck cancers are treated.

2.5 Guidelines

The guidelines were developed based on the literature while remaining cognisant of the variation in treatment delivery and imaging capacities of radiation therapy departments across Europe.

CHAPTER 3: SURVEY RESULTS

3.1 Characteristics of respondents

A total of 187 responses were received, from 24 of 32 invited countries. Germany (34 respondents, 18.2%), the UK (30 respondents, 16%) and Greece (23 respondents, 12.3%) were the three largest contributors. Several countries contributed small numbers of surveys with15 countries returning fewer than 5 surveys: see Figure 1. However, it should be noted that for smaller countries, the response rate was extremely high, such as in Cyprus (100%), The Netherlands (78%) (18 from 23 departments) and Ireland (75%) (9 from 12 departments).

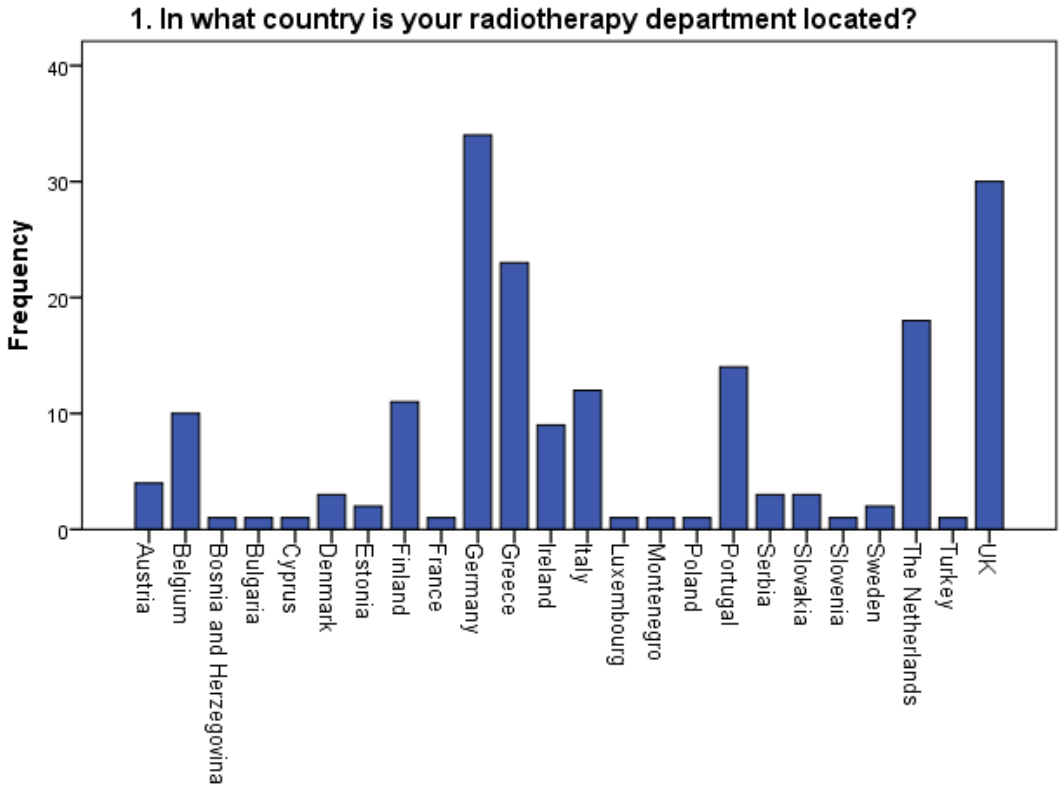

Figure 1. Country of origin of respondents

The profession of the respondents was overwhelmingly Radiation TherapisT (RTT). The principal exception being the Greek respondents, all of whom were Radiation Oncologists (RO) or RO trainee (N=23), and were counted as "Other" as seen in Figure 2.

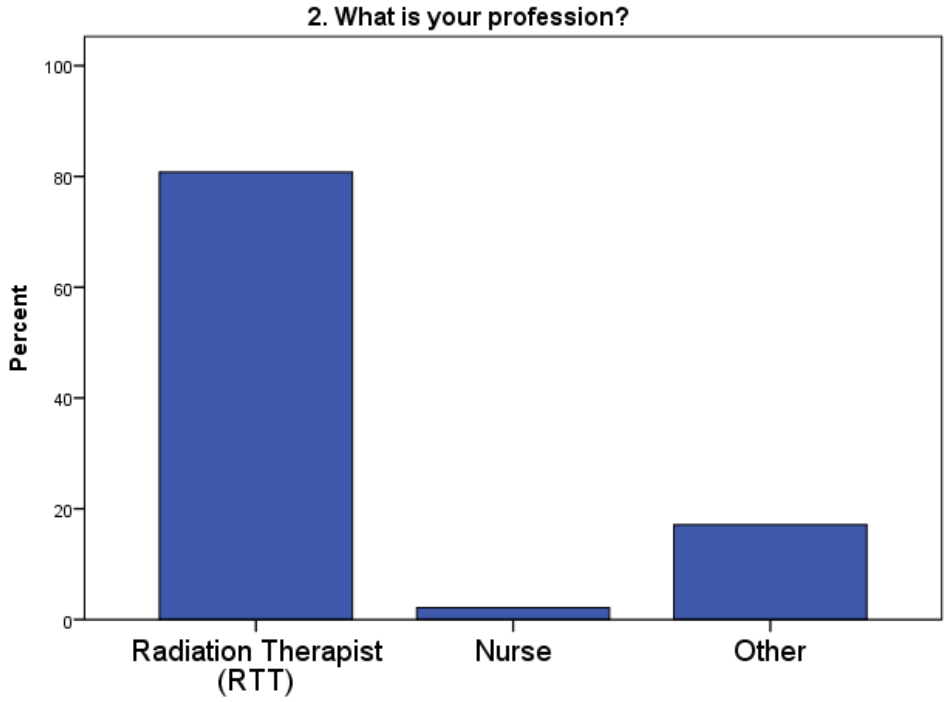

Figure 2. Profession of Respondents

The majority of responding departments reported seeing fewer than 500 head and neck patients annually (Figure 3). Germany and a number of smaller countries such as the Netherlands, Greece and Serbia reported treating higher numbers (Figure 4).

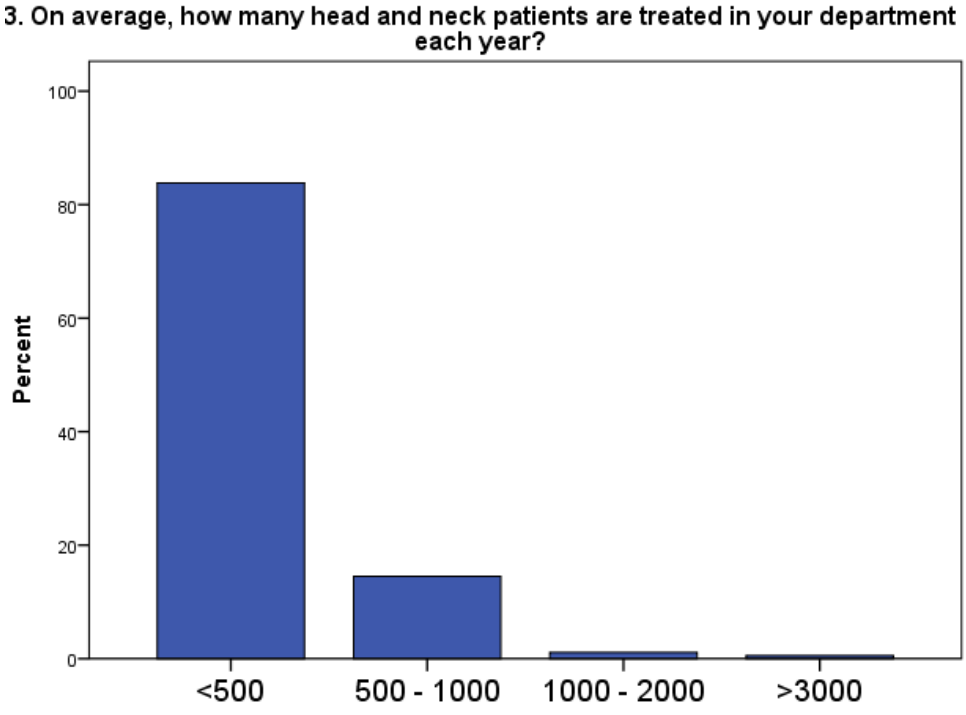

Figure 3. Number of Head and Neck Patients treated per annum

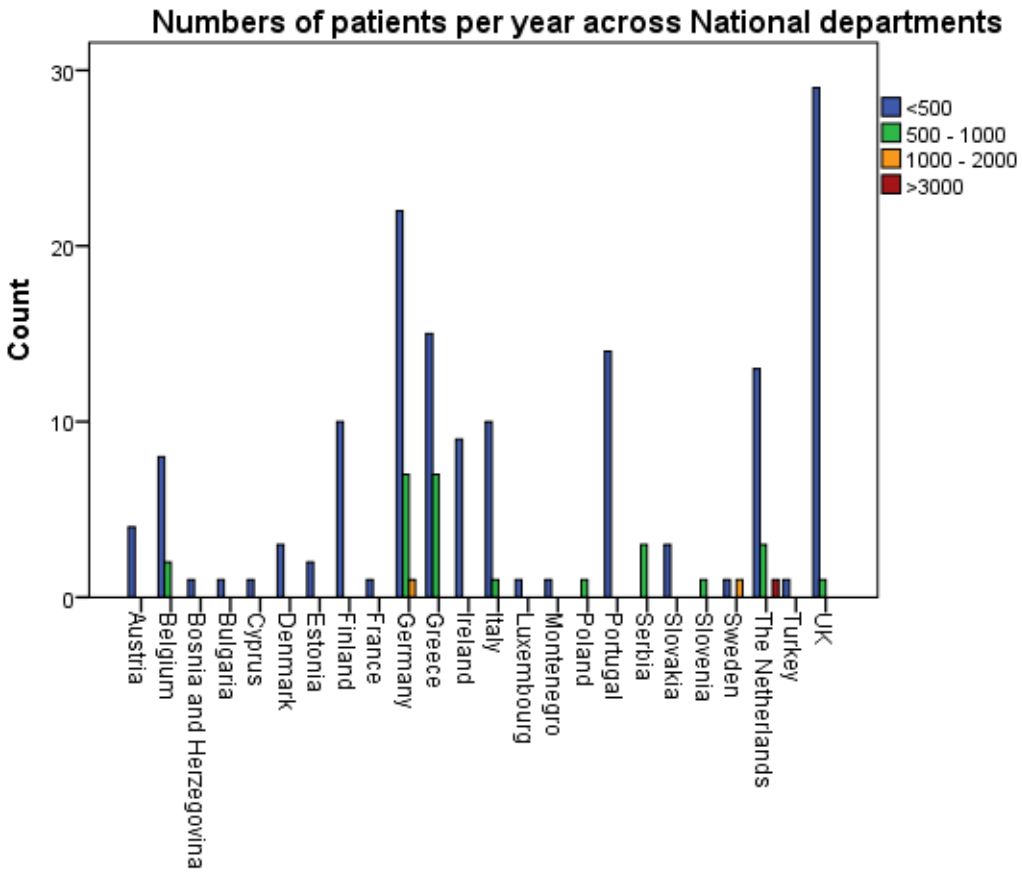

Figure 4. Number of Head and Neck Patients treated per country per annum

3.2 Patient positioning

3.2.1 Initial Patient Positioning

The majority of initial patient positioning was performed at CT (Figure 5).

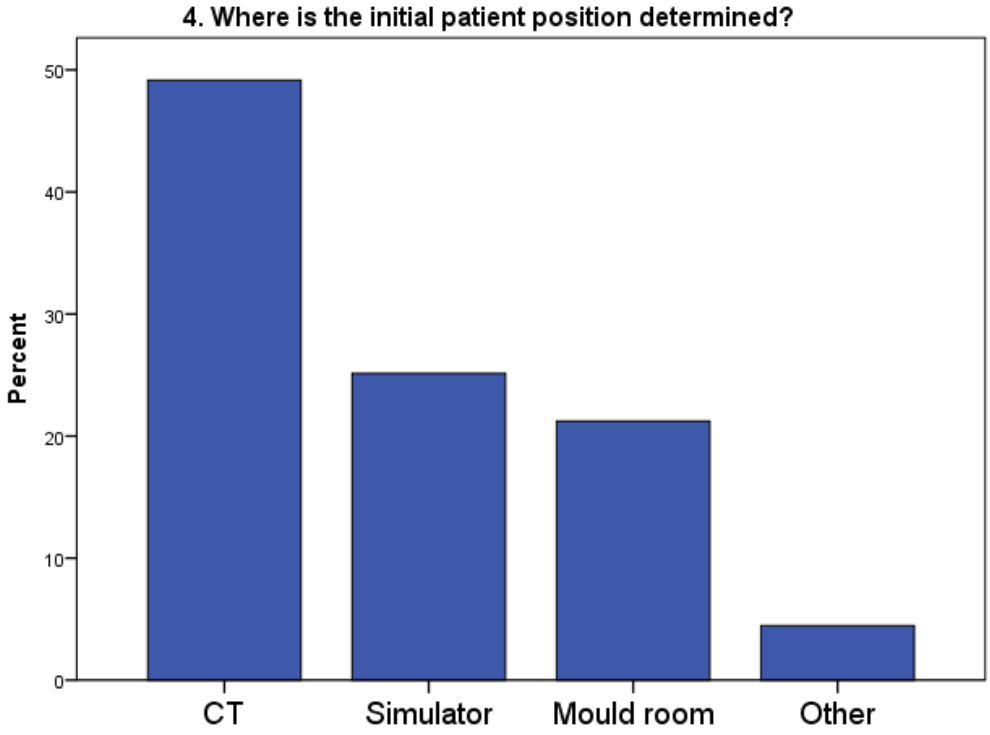

Figure 5. Location of initial patient positioning

In 73 responding departments (42%) the decision on selecting the patient position was taken by a single person, primarily the RTT (N=30, 17%) or the RO (N=33, 19%).

When more than one person was involved in the decision, either the RTT or the RO or both were always involved. In 92 instances (53%) both the RTT and the RO were involved and occasionally involving the Physicist (N=16, 8.6%), the Dosimetrist (N=3, 2%) or the Mould Room Technician (N=1, 0.6%). All responses are given in Table 1.

Table 1. Responsibility for determining Patient Position

Decision by:	N	%
RTT	30	17.1
Physicist	1	0.6
RO	33	18.9
Nurse	2	1.1
Other	7	4.0
RTT + RO	72	41.1
RTT + Physicist + RO	16	9.1
RO + Physicist	3	1.7

Decision by:	N	%
RO + Mould room technician	1	0.6
RTT + Mould room technician	3	1.7
RTT + RO + Dosimetrist	3	1.7
RTT + Nurse	1	0.6
RO + Nurse	2	1.1
RTT + RO + Mould room technician	1	0.6
Total	*175*	
No response	12	

3.2.2 Positioning and Immobilisation Protocols and Workflow

The majority of patients are asked to remove their upper clothing prior to positioning and immobilisation.

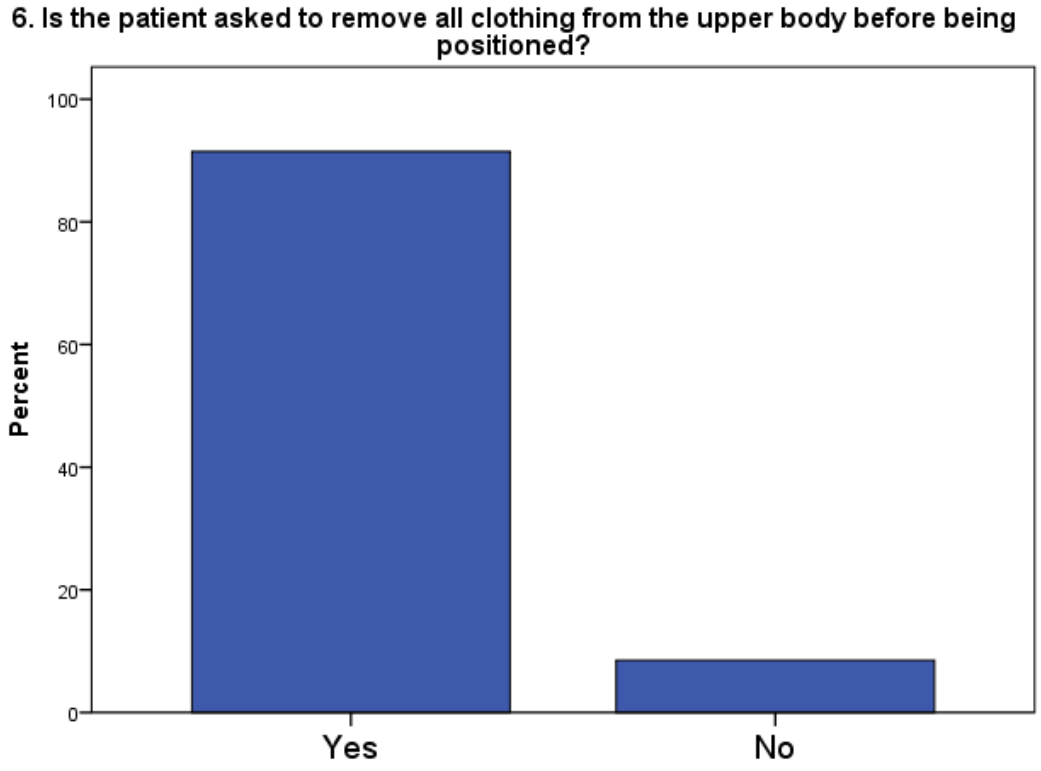

Figure 6. Removal of upper clothing prior to positioning

The majority of respondents stated that an institutional protocol was followed when positioning and immobilising head and neck patients. (Figure 7), this was further analysed per country (Figure 8). 66.7% of protocols were site-specific within the head and neck, but 33.3% were not (Figure 9).

The RTT and RO were primarily involved in the drafting of such protocols, followed by contributions from the Physicist.

For 48 responses (32.7%) a single person was responsible for writing the protocol. The majority of these were the RTT (N=27, 18.4%) or the RO (N=17, 11.6%), with the Physicist writing it alone in only 4 cases (2.7%).

The other 99 responses (67.3%) involved two or more persons writing the protocol. These always included the RTT, (N=10, 6.8%) the RO (N=4, 2.7%) or both (N=85, 57.8%).

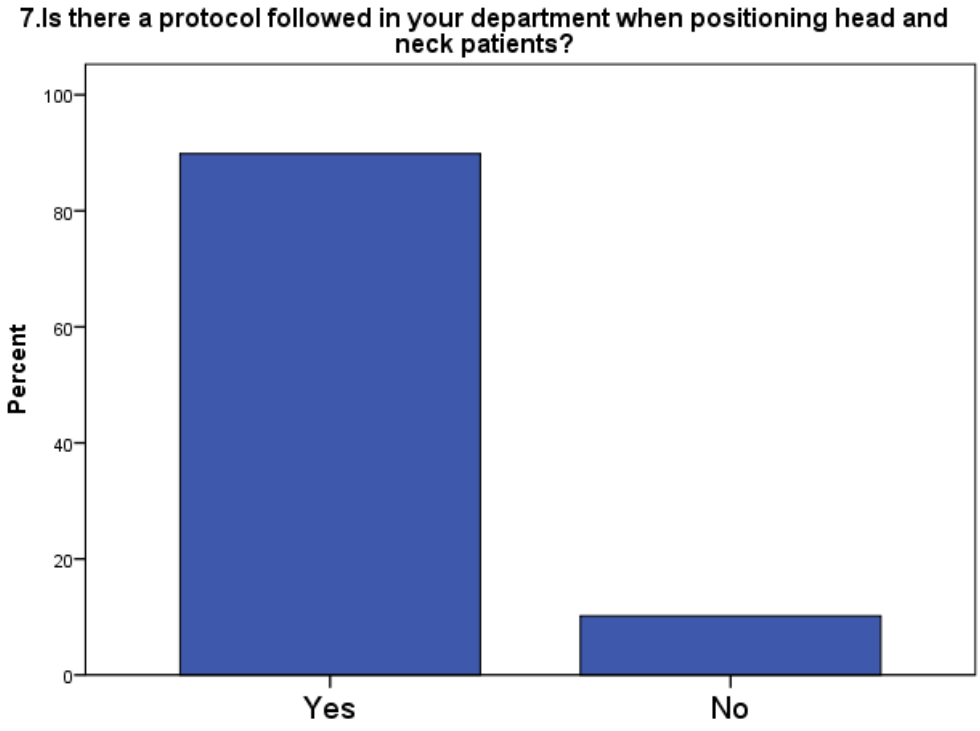

Figure 7. Presence of protocol for positioning and immobilisation of head and neck patients

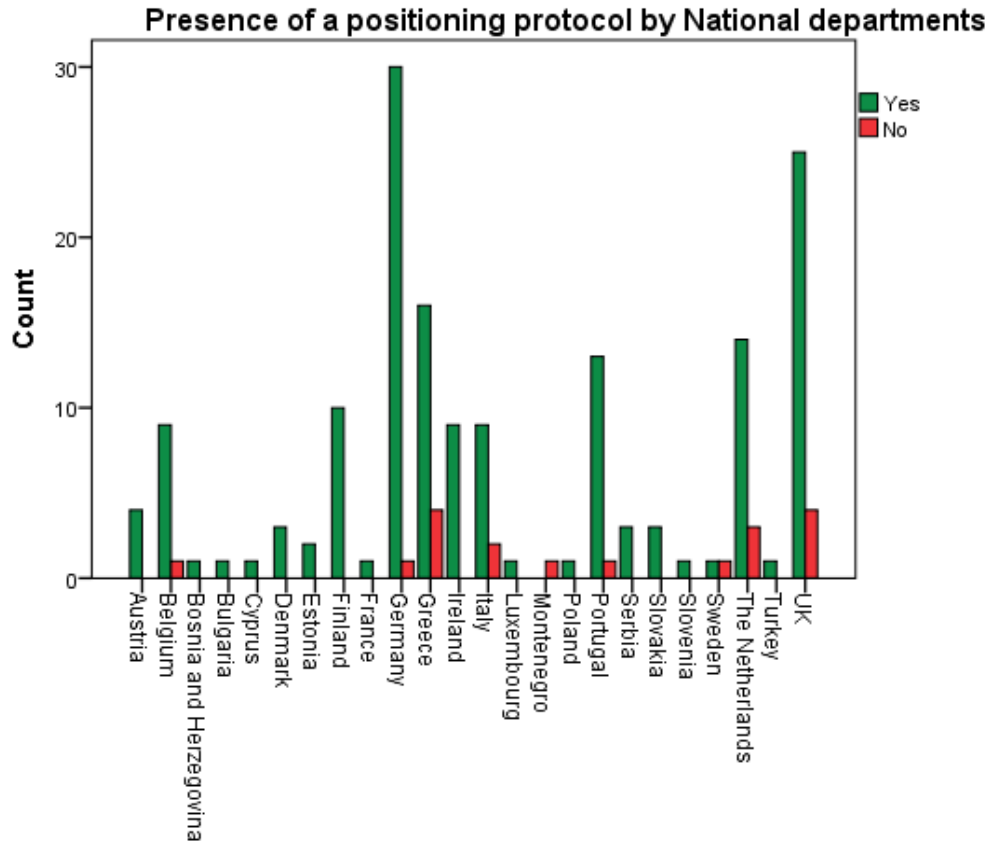

Figure 8. Presence of a positioning protocol by country

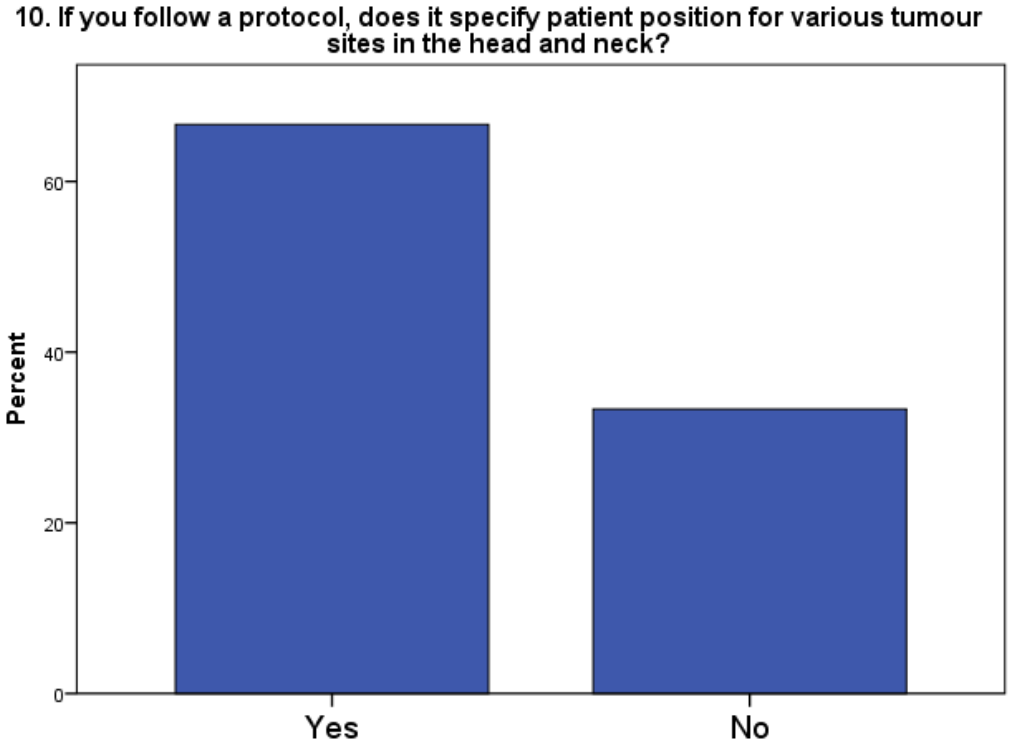

Figure 9. Presence of site-specific positioning and immobilisation protocol

Respondents were asked to specify the reference points they used when positioning and immobilising head and neck patients.

The majority of respondents reported using more than one reference point (N=157, 90.8%).

- 30 respondents (17.3%) used two reference points.
- Three reference points were used by 57 (32.9%) of respondents, mostly nose and chin and either shoulders (N=15) or forehead (N=19).
- Four reference points were used by 45 respondents (26.0%), predominantly nose, chin, forehead and shoulders (N=30).

The other 25 respondents (14.5%) also used those reference points, in addition to the ears.

Shoulder and arm positions were maintained solely by the patient themselves in 68.5% of departments, with minimal use of shoulder retractors or other such devices reported.

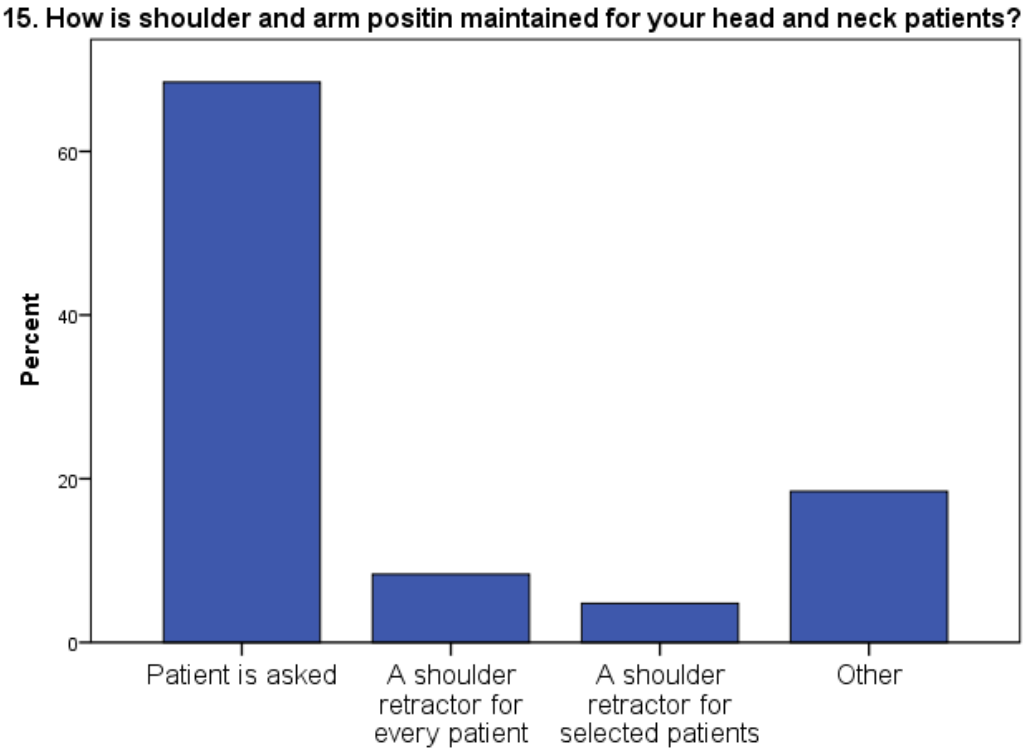

Figure 10. Maintenance of shoulder and arm position

3.3 Immobilisation Devices

3.3.1 Mask Type

The majority of responses indicated that a single mask type was used (N=106, 64.2%), including 68 (41.2%) who use a 5-point mask exclusively. Of those using two mask types, most favoured 3-point and 5-point masks (N=23, 13.9%). Only 2 respondents (1.2%) reported using 3, 4 or 5-point masks.

Table 2 illustrates mask type by country counting the usage of each mask type separately (total sum is greater than the number of responders, as several responding centres use more than one mask type):

3.3.2 Immobilisation Device Protocols

In 72.6% of cases, the mask selection was protocol-led (Figure 11) and was site specific in 65.5% of respondents' departments (Figure 12). 65.6% of respondents stated that a mask selection protocol would increase consistency in their departments (Figure 13).

Table 2. Mask type by country

Country	3-point	4-point	5-point	Other	Total
Austria	1 (33.3%)	0	0	2 (66.7%)	3
Belgium	0	0	10 (100%)	0	10
Bosnia and Herzegovina	0	0	1 (100%)	0	1
Bulgaria	1 (100%)	0	0	0	1
Cyprus	1 (100%)	0	1 (100%)	0	1
Denmark	1 (33.3%)	0	1 (33.3%)	1 (33.3%)	3
Estonia	2 (100%)	0	2 (100%)	0	2
Finland	3 (37.5%)	1 (12.5%)	6 (75%)	1 (12.5%)	8
France	0	0	1 (100%)	0	1
Germany	14 (46.7%)	9 (30%)	13 (43.3%)	2 (6.7%)	30
Greece	7 (50%)	7 (50%)	5 (35.7%)	0	14
Ireland	3 (33.3%)	1 (11.1%)	6 (66.7%)	1 (11.1%)	9
Italy	1 (10%)	4 (40%)	2 (20%)	3 (30%)	10
Luxembourg	0	0	1 (100%)	0	1
Montenegro	1 (100%)	0	0	0	1
Poland	0	0	1 (100%)	0	1

Country	3-point	4-point	5-point	Other	Total
Portugal	7 (50%)	2 (14.3%)	11 (78.6%)	2 (14.3%)	14
Serbia	1 (33.3%)	0	3 (100%)	0	3
Slovakia	1 (33.3%)	2 (66.7%)	1 (33.3%)	0	3
Slovenia	0	0	1 (100%)	0	1
Sweden	2 (100%)	0	0	0	2
The Netherlands	3 (18.8%)	1 (6.2%)	16 (100%)	0	16
Turkey	1 (100%)	0	0	0	1
UK	6 (20.7%)	0	15 (51.7%)	11 (37.9%)	29
Total	56 (33.9%)	27 (16.4%)	97 (58.8%)	23 (13.9%)	165

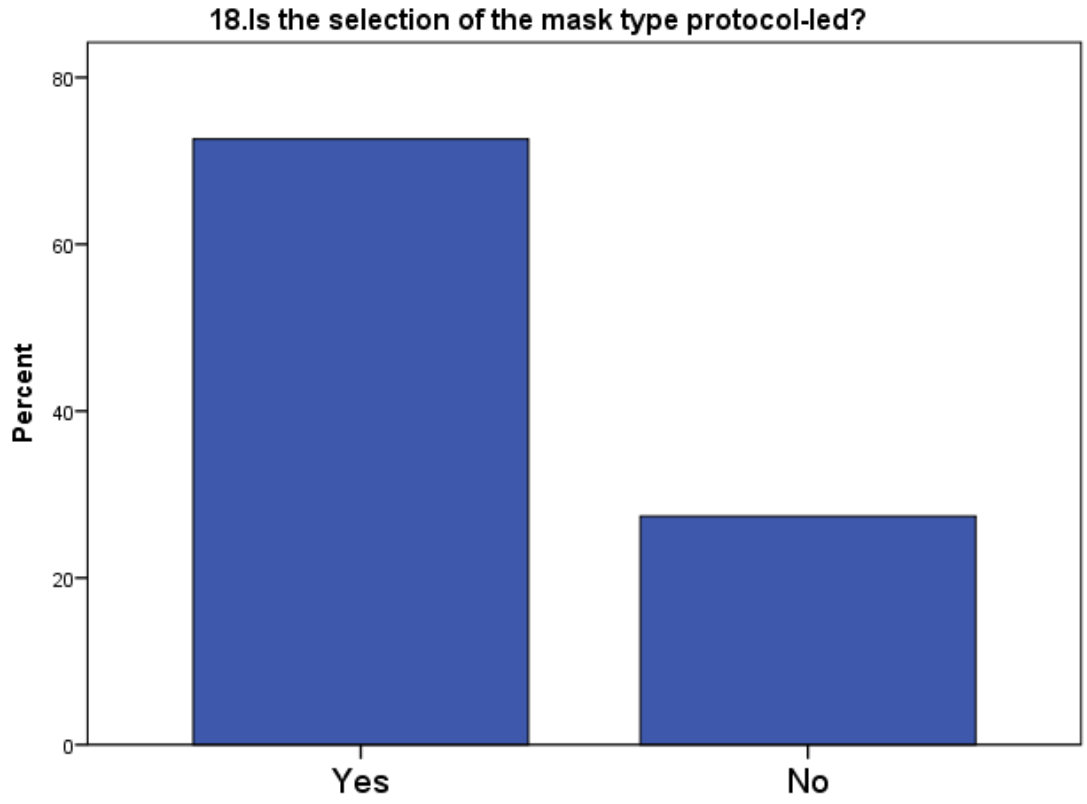

Figure 11. Mask selection Protocol

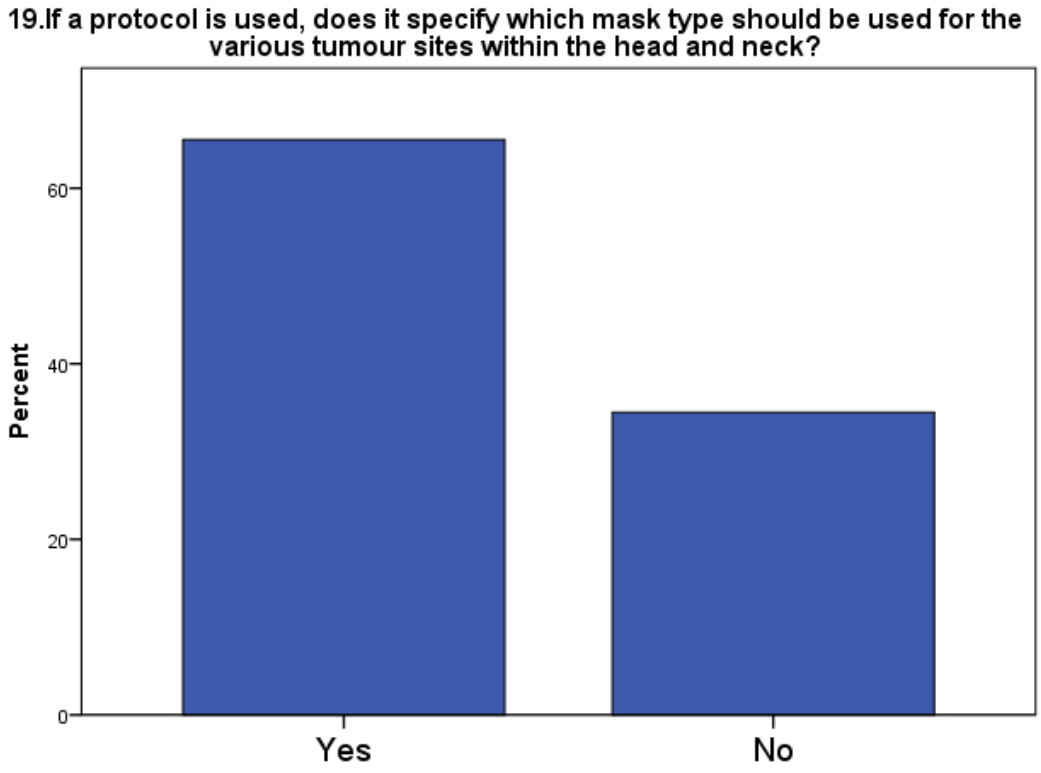

Figure 12. Site-specific mask type given in protocol

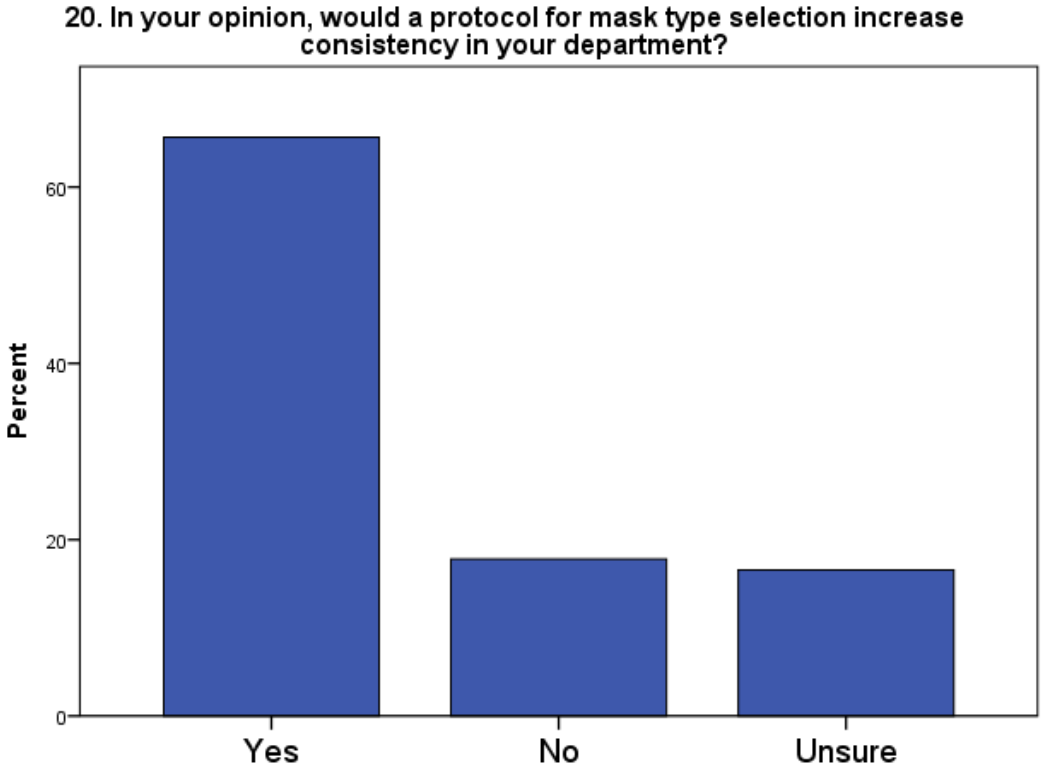

Figure 13. Mask selection protocol and increase in consistency

In the majority of cases, a single professional selects the mask to be used: the RTT (N=44, 27.5%), the RO (N=35, 21.9%), the nurse (N=3, 1.9%), or another (N=14, 8.8%).

If two or more people select the masks, this always includes the RTT (N=11, 6.9%) or the RO (N=11, 6.9%), or both the RTT and the RO (N=48, 30.0%).

3.3.3 Indexing of Immobilisation Devices

Table 3 illustrates the locations where the immobilisation system is reported as being fixed (indexed) to the treatment couch in each area identified. The counts (and percentages) are not mutually exclusive, so will not sum to the totals. Only a minority of centres (7.1%) report that the immobilisation system is not indexed either at pre-treatment or on-treatment.

Table 3. Indexing of immobilisation system

Is immobilisation system fixed to the treatment couch in:	N	Percent
Mould room	39	23.2
Simulator	65	38.7
CT	142	84.5
Linear accelerator	140	83.3
None of the above	12	7.1
Total responses	*168*	
No response	19	

3.3.4 Neck-rest Selection

The majority of centres stated that they used a combination of standard and customised neck rests (40.4%), 11.8% of centres stated that they used 'other' neck-rests, with some being constructed in-house and others using a stereotactic set up (Figure 14).

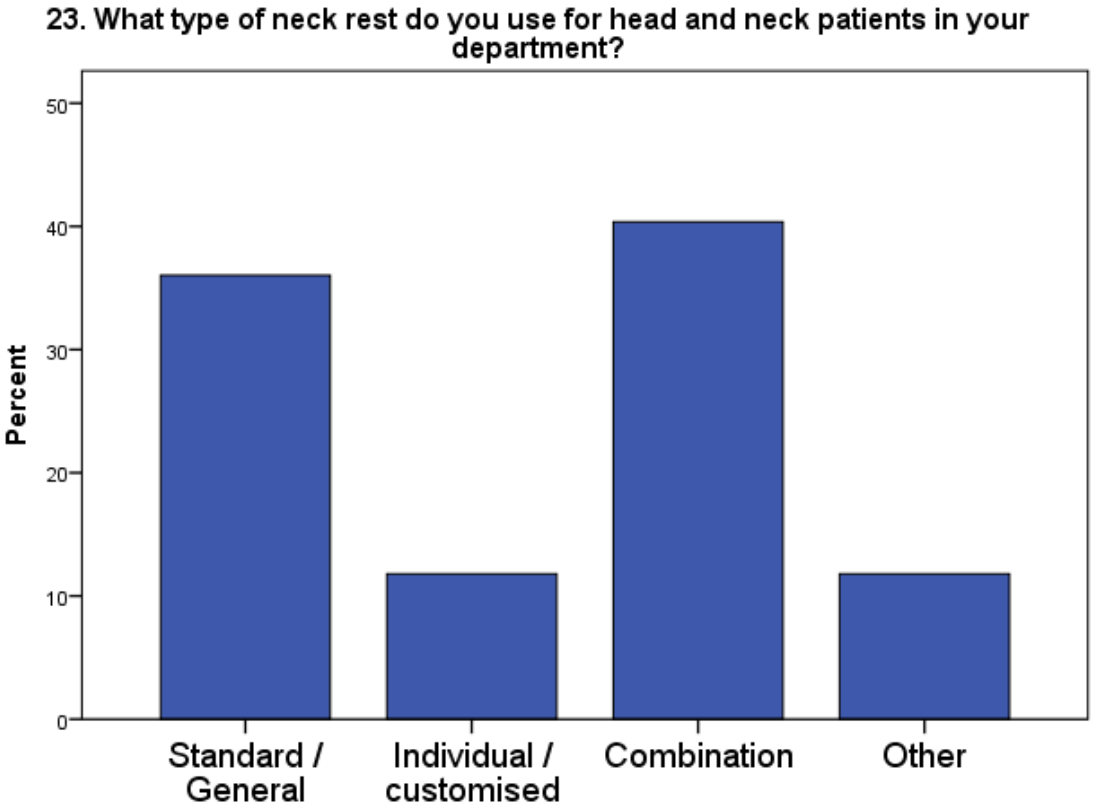

Figure 14. Neck rest type

3.4 CT / Simulation practices

3.4.1 Treatment Technique

The most commonly reported technique used to treat the majority of head and neck patients was IMRT (48.5%), followed by 3DCRT (27.9%). VMAT was used to a lesser extent and 2D techniques are now almost obsolete (2.4%) as given in Figure 15.

For IMRT and VMAT treatments, a combination of standard and customised neck rests was most commonly used (44.7% and 53.3%, respectively). For 3DCRT treatments, standard neck rests were most commonly used (53.3%). Full results are given in Table 3.

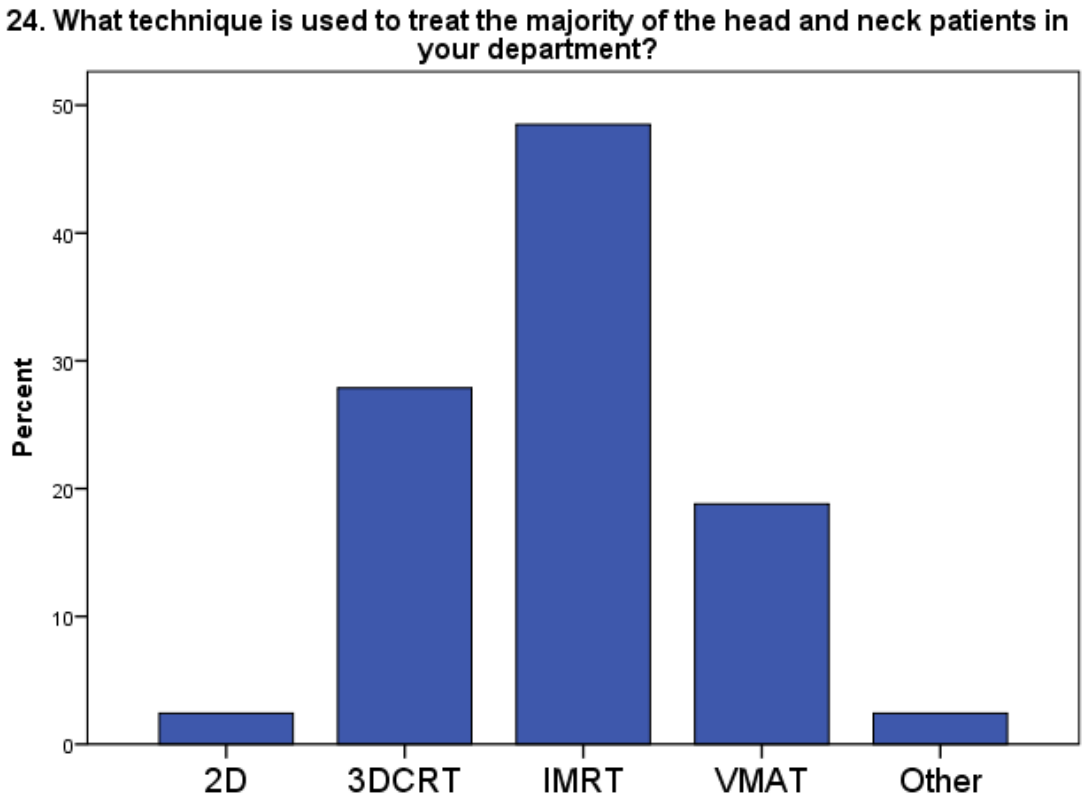

Figure 15. Treatment technique most commonly used for HNC patients

Table 4. Treatment Technique versus Neck Rest Type

	Type of neck rest used				
Treatment technique	**Standard / General**	**Individual / customised**	**Combination**	**Other**	**Total**
2D	2 (66.7%)	0	1 (33.3%)	0	3
3DCRT	24 (53.3%)	6 (13.3%)	10 (22.2%)	5 (11.1%)	45
IMRT	25 (32.9%)	9 (11.8%)	34 (44.7%)	8 (10.5%)	76
VMAT	6 (20%)	2 (6.7%)	16 (53.3%)	6 (20%)	30
Other	1 (25%)	2 (50%)	1 (25%)	0	4
Total	58 (36.7%)	19 (12.0%)	62 (39.2%)	19 (12.0%)	158

3.4.2 CT Procedures

For all treatment techniques, the most commonly used axial slice thickness at CT was 3 mm. In 35.5% of VMAT cases, 2.5 mm slice thickness was reported, as illustrated in Figure 16.

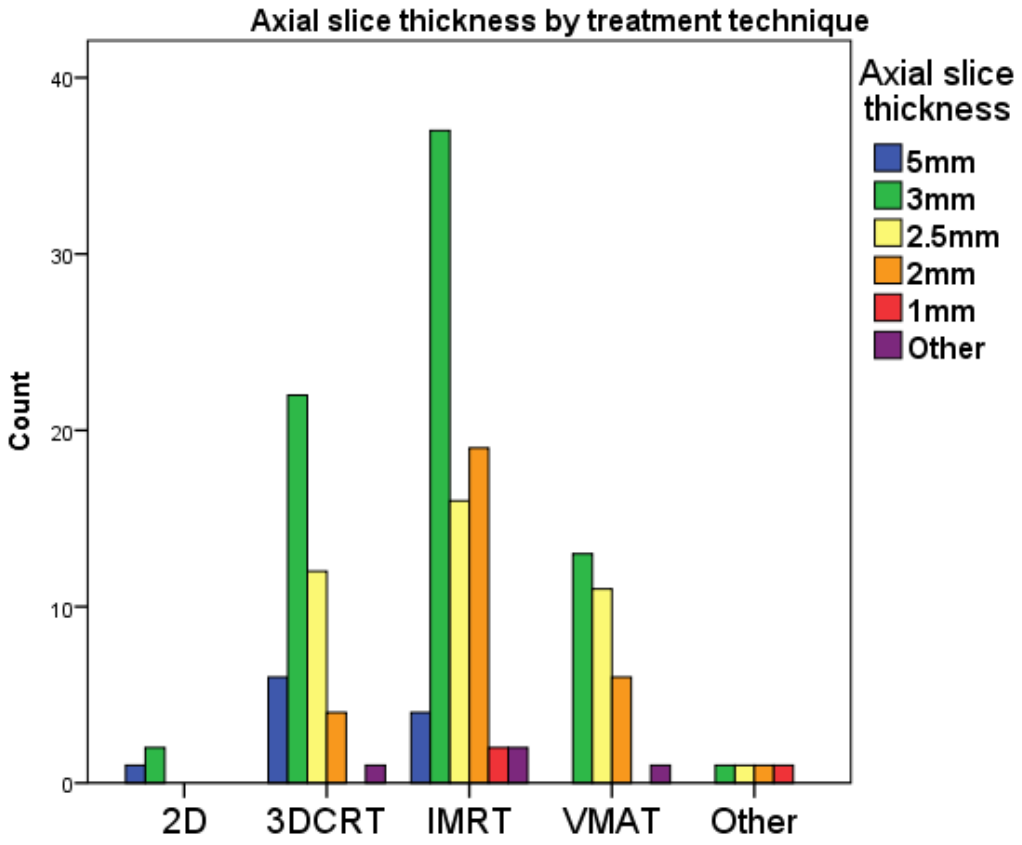

Figure 16. Treatment technique versus Axial Slice Thickness

There was no consensus on the use of contrast at CT. 41% of respondents performed planning CTs with contrast, while 37.2% did not. 21.8% used contrast only on occasion.

Similarly, no consensus was observed on the routine taking of a new CT scan during treatment with 52.4% of respondents stating that new CT scans were routinely taken while 47.6% did not routinely take a new CT scan during treatment.

3.5 Position Verification

3.5.1 On-treatment Imaging Modalities

In total, 83 (51.2%) respondents use only one modality, predominantly CBCT (N=24, 14.8%) or MV EPIs (N=25, 15.4%). A further 57 respondents (35.2%) reported using more than one modality, mostly comprising CBCT and MV EPIs (N=19, 11.7%) or one of those with kV EPIs. A similar number use all three of the most popular modalities: CBCT and kV EPIs and MV EPIs (N=15, 9.3%), with much fewer respondents using other combinations of three or four modalities.

92.1% of respondents followed an image guidance protocol for HNC patients. The position verification method used was also cross-tabulated with the treatment technique used (Table 4) and the full range of methods used is given in Table 5.

Table 5. Position verification method vs. treatment technique

Imaging modality used to verify positioning	N (percent) of treatment techniques					
	2D	3DCRT	IMRT	VMAT	Other	Total
Cone beam CT	3 (3.6%)	13 (15.7%)	44 (53%)	21 (25.3%)	2 (2.4%)	83
kV EPIs	1 (1.6%)	15 (24.2%)	29 (46.8%)	17 (27.4%)	0	62
MV EPIs	1 (1.4%)	24 (32.4%)	43 (58.1%)	5 (6.8%)	1 (1.4%)	74
MV Portal films	1 (2.9%)	19 (54.3%)	13 (37.1%)	2 (5.7%)	0	35
CT on rails	0	0	2 (50%)	1 (25%)	1 (25%)	4
Other	0	0	2 (66.7%)	0	1 (33.3%)	3
Total	3 (1.9%)	46 (28.7%)	77 (48.1%)	30 (18.8%)	4 (2.5%)	160

Table 6. Position Verification Method

Imaging modality used to verify position	N	%
MVCT	3	1.9
CT on rails	4	2.5
kV EPIs	13	8.0
MV Portal films (PFs)	14	8.6
Cone beam CT (CBCT)	24	14.8
MV EPIs	25	15.4
MV EPIs + PFs	3	1.9
CBCT + PFs	5	3.1
kV EPIs + PFs	6	3.7
kV EPIs + MV EPIs	10	6.2
CBCT + kV EPIs	14	8.6
CBCT + MV EPIs	19	11.7
CBCT + MV EPIs + PFs	1	0.6
CBCT + kV EPIs + PFs	3	1.9
CBCT + kV EPIs + MV EPIs	15	9.3
CBCT + kV EPIs + MV EPIs + PFs	3	1.9
Total	162	
No response	25	

3.5.2 Position Verification Protocols

Participants were asked to give details of the protocol used. From this the action level of the correction protocol (Figure 17) and the type of correction protocol were extracted (Figure 18).

The action levels reported are listed below. There was deviation from a single response in that some respondents, who use a 3 mm level for 3D CRT, reduce this to 2 mm for IMRT (N=2, 2%) or 0 mm for IMRT/VMAT (N=1, 1%). Therefore the numbers and percentages will not sum to the total as shown in Figure 17. Note that '0 mm action level' refers to daily online imaging and matching, however on-line matching with an action level was also reported.

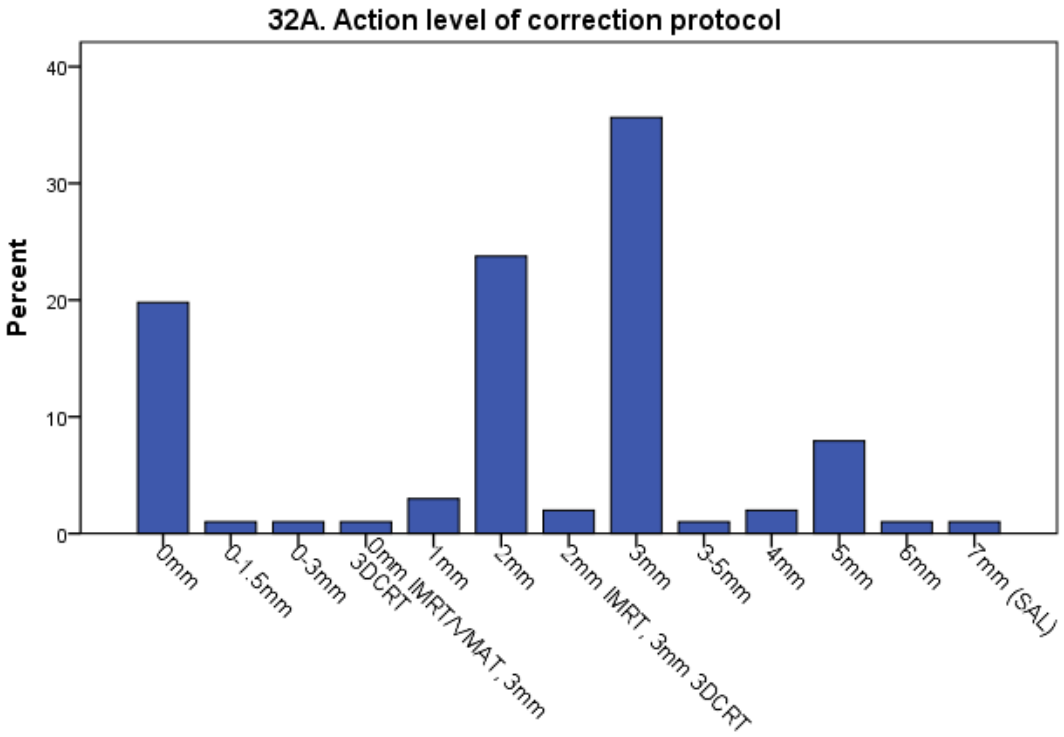

Figure 17. Action Level of correction Protocol

The type of protocols reported were coded into those using defined time periods, those using defined fraction numbers, those who used a combination of time periods and fraction number, and "other". For a breakdown of each of these categories, see Figure 18.

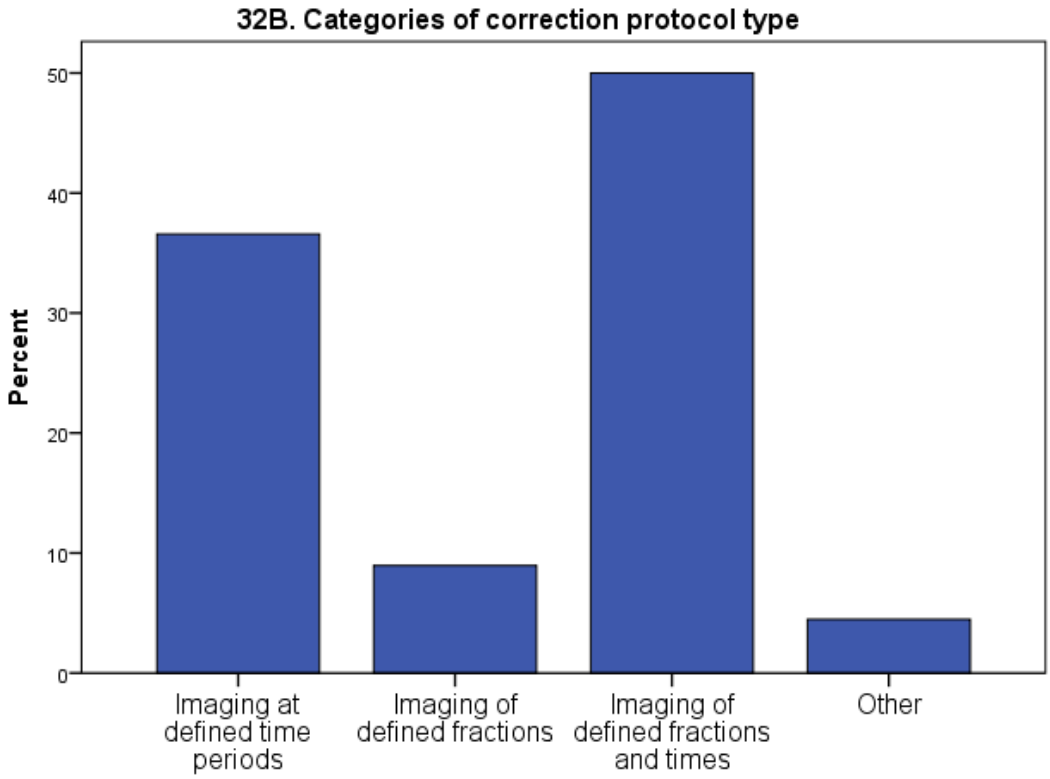

Figure 18. Coded categories of correction protocol

The above categories broke down as follows in Tables 7-10.

Table 7. Protocols based on defined time periods

Imaging at Time periods:	N	%
Daily (online)	34	25.4
2-3 times per week	3	2.2
Day 1, then weekly	2	1.5
Day 2, then weekly	1	0.7
Once per week	6	4.5
Twice per week	1	0.7
Days 1-6, 11-16	1	0.7
Every 2 weeks	1	0.7
Total	49	36.6

Table 8. Protocols based on defined fraction number

Imaging at Fractions:	N	%
Every 3 fractions	1	0.7
First 3 fractions	5	3.7
First 3 fractions, fractions 10 & 15	1	0.7
First 3 fractions then every 2nd fraction	2	1.5
First 4 fractions	3	2.2
Total	12	9.0

Table 9. Imaging at defined time periods and fraction numbers

Imaging at Time periods and fractions:	N	%
First 2 fractions, then weekly	5	3.7
First 3 fractions, then weekly	42	31.3
First 3 fractions, then daily/weekly	3	2.2
First 4 fractions, then weekly	5	3.7
First 5 fractions, then weekly	4	3.0
Days 1-5, then every 3rd fraction	2	1.5
Days 1-2, then every 4th/5th fraction	4	3.0
Day 1, then every 5th fraction	1	0.7
Daily for IMRT/VMAT, First 3 fractions, then weekly for 3DCRT	1	0.7
Total	67	50.0

Table 10. Other defined protocols

Imaging protocols:	N	%
SAL, 3 fractions	2	1.5
Combination of SAL and NAL	1	0.7
Combination of online & offline	3	2.2
Total	*6*	*4.5*

To elucidate relationships between the protocol type and action level, a cross-tabulation was performed in Table 11.

Table 11. Protocol Type versus Action Level

Imaging at:	0mm	0-1.5mm	0-3mm	1mm	2mm	3mm	3-5mm	4mm	5mm	6mm	7mm
Defined times	20 (19%)	0	0	3 (3%)	10 (10%)	8 (8%)	1 (1%)	0	1 (1%)	0	0
Defined fractions	0	0	0	0	2 (2%)	1 (1%)	0	0	2 (2%)	0	0
Both	1 (1%)	0	0	0	14 (13%)	30 (29%)	0	2 (2%)	4 (4%)	1 (1%)	0
Other	0	1 (1%)	1 (1%)	0	0	0	0	0	1 (1%)	0	1 (1%)
Total	*21*	*1*	*1*	*3*	*26*	*39*	*1*	*2*	*8*	*1*	*1*

As can be seen in the previous tables, the majority of protocol types are "Daily" and "First 3 fractions, then weekly", indicative of the e-NAL offline protocol. The "Daily" protocols mostly use 0mm (daily online matching), while the "First 3 fractions, then weekly" mostly use an action level of 3 mm, with about one third using an action level of 2 mm.

3.6 Quality Assurance

Over 77% of respondents checked the fit of the patient's thermoplastic mask each day (Figure 19)

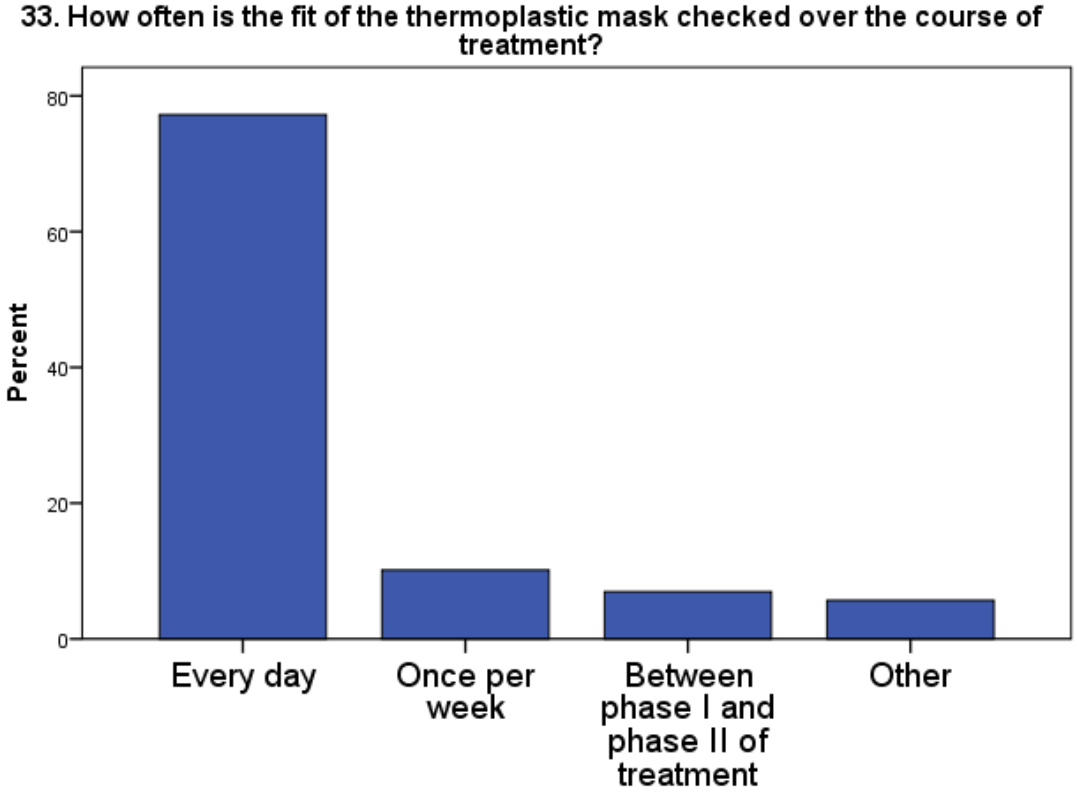

Figure 19. Frequency of checking thermoplastic mask fit

Only 14.2% of respondents stated that they re-used thermoplastic masks in their department with the majority of respondents stating that they were not re-used for infection control purposes.

CHAPTER 4: EVIDENCE-BASED POSITIONING, IMMOBILISATION AND POSITION VERIFICATION FOR HNC PATIENTS.

Reviewing the literature indicates that there has been substantial changes in the set up, positioning, immobilisation and verification of head and neck cancer patients over the last number of decades. This has included evaluation of head and neck support cushions and comparison of immobilisation systems, both commercial and in-house, usually through the quantification of set-up errors. In some cases, these errors are further categorised into systematic and random components and various image guidance measures are also described.

4.1 Positioning and Immobilisation

4.1.1 Immobilisation Systems for HN RT

Many authors have evaluated a range of immobilization systems for head and neck patients. Many report on retrospective single-arm studies while others compare and evaluate two systems in prospective, randomized controlled trials.

As far back as 1997, it was recognised by Bentel (27) that in order to improve reproducibility in the treatment of head and neck and brain tumour patients, the immobilisation system had to be indexed or fixed to the treatment couch. This was a retrospective study that analysed isocentre shifts on a weekly basis using portal films for 68 head and neck and 72 brain tumour patients.

Hong et al (28) prospectively analysed 20 patients with locally advanced head and neck cancer. All patients were immobilised with a thermoplastic mask and a maxillary bite tray, in which 4 fiducial markers were implanted for image guidance of translations and rotations around the isocentre. 10 patients were treated with 3DCRT and 10 with an IMRT technique. The mean absolute set up error in any single dimension was 3.3 mm. With 6 degrees of freedom, a mean set-up deviation of 6.9 mm (SD 3.6 mm) was found. When put into a planning context, this deviation would mean a 20-30% PTV underdosage, relative to dose specification, using an IMRT technique.

In a large series, Sharp et al (29) prospectively compared two different immobilisation systems in 241 patients with various primary tumours in the head and neck. The immobilisation systems were a thermoplastic head mask or a head and shoulder mask (Posicast) fixed on a carbon fibre base-plate (Posifix) with a foam head support. All patients were treated with a 3DCRT technique. 15% of patients in both groups had their masks cut out either due to intense erythema or excessive tightness of fit. 5 patients had new masks made due to instability; these patients had either a head mask or a head and shoulder mask. Portal images were acquired at two endpoints; first after treatment commencement and once again after 4 weeks. Portal and simulator images were compared, as were differences in actual treatment table positions. It was concluded that there was no difference between

the immobilisation systems in the number of shifts or in the number of setup errors, as measured by the table positions.

Karger (30) reported on 4 patients treated with particle therapy for base of skull tumours, who were immobilised using an in-house developed system consisting of a cast made of self-hardening bandages attached to a stereotactic frame. Markers used to ascertain reproducibility of this stereotactic set included isocentre match, matching of implanted fiducials within the skull as well as the matching of two 2mm metal balls that were glued to the upper and lower sides of the mask. Overall, stereotactic CTV-PTV margins of 1-2mm were achieved using this device.

Willner (31) reported on the data of 29 ear, nose and throat patients who were immobilised using an individual bite-block fixation device with a semi-standardised head and neck rest support. Patients were treated with a combination of two arc fields and two oblique wedged fields with a common isocentre positioned at the posterior border of the spinal cord. Arc fields were offset beyond the central axis so that the spinal cord always lay outside of the field. Patient position was verified four to six times over the course of treatment using bony anatomy close to the isocentre. Total systematic displacement was quantified as 1.9-2.1 mm while total random displacement was given as 1.8-2.2mm.

In 2007, McKernan et al (32) reported on prospective data from 120 patients with head and neck cancer who were immobilised using a rigid cast made either from traditional Plaster of Paris bandages or from data acquired using a laser scanner. The fitting of the cast was evaluated by RTTs using reference points such as the chin, nose and superior skull. The mask preparation with the laser scanner took 15 minutes fewer than for the plaster of Paris method (60 minutes versus 75 minutes). RTT opinion was sought on mask function including the fit of the mask, its daily reproducibility as well as patient immobilisation and patient comfort. The RTTs were also asked to comment on the ease of mask production, mask accuracy as well as patient tolerance. For all categories, RTTs reported the laser scanner method was preferable to the Plaster of Paris method.

In 2006, Boda-Heggmann et al (33) reported on prospective data of 21 head and neck cancer patients who were immobilised either in a thermoplastic mask or a rigid cast mask. Patients were treated either with 3DCRT or IMRT with a stereotactic set up. Position verification was performed using daily CBCTs with automatic matching based on intracranial regions or on cervical vertebrae. The most favourable alignment of the neck region was observed with the addition of shoulder and thoracic tattoos for the rigid system. For the rigid mask, improvements from 1.79 ± 4.79 mm to -0.8 ± 2.4 mm were observed in the AP direction, from 2.25 mm ± 2.41 mm to -0.4 mm ± 1.9 mm in the CC direction and -1.58 mm ± 2.07 mm to 0.43 mm ± 2.58 mm in the lateral direction. Roll and yaw were also slightly improved but pitch remained similar. However, for both systems, neck repositioning was inferior to that of the intracranial region. The most significant difference between the two systems was observed in the alignment of the neck region in the CC direction, which was 4.07 mm ± 5.1 mm for the thermoplastic mask compared to -0.4 mm ± 1.9 mm with the rigid mask and tattoos.

Donato et al (34) reported on 20 head and neck cancer patients who were immobilized either in a 3-point rigid mask (Uvex) or a thermoplastic mask (Ultraplast). The time to construct the rigid mask was 181 minutes, versus 42.4 minutes for the thermoplastic mask; this included the work of two RTTs as well as the time required to educate the patient on the procedure. All patients were treated with a 3DCRT technique. Daily EPIs were acquired on the right lateral image only and bony matching to vertebrae was performed. The rigid mask resulted in a systematic error of 2.6 mm compared to 1.9 mm for the thermoplastic mask in the AP direction. Results were similar in the CC direction; 1.6 mm for the rigid mask compared to 1.8 mm to the thermoplastic mask. Pitch was also measured and was reported as 1.3° (SD) for the rigid mask and 1.6° (SD) for the thermoplastic mask. Mixed results were observed for random deviations with 1.9 mm being observed in the AP direction for the rigid mask, compared to 2.3 mm for the thermoplastic mask. Conversely, a more favourable 2.2 mm random deviation in the CC direction was reported for the thermoplastic system, relative to the 3.8 mm reported for the rigid system. However, the standard deviation of the random pitch recorded for the rigid mask was 1.8° compared to 2.1° for the thermoplastic mask.

Humphreys et al (35) reported on 20 patients treated for a variety of head and neck primary tumours that were immobilised in a four-point customised rigid mask system (Cabulite). Patients were treated with an IMRT technique and were verified using orthogonal EPIs daily for the first week of treatment and subsequently weekly. Stable anatomical structures were used in automatic matching between the reference and electronic portal images. Systematic deviations of 0.02 mm, 0.7 mm and 0.9 mm were reported in the AP, CC and lateral directions as well as a pitch of 0.5° and yaw of 0.2°. Random errors were reported as standard deviations of ±0.7 mm, ±0.6 mm and ±0.4 mm in the AP, CC and lateral directions. Pitch was ±0.3° and yaw was ±0.2°. From these data, the CTV to PTV expansion required for this immobilisation system was calculated using the van Herk formula as being 3.3 mm in the AP direction, 2.6 mm in the CC direction and 2.9 mm in the lateral direction.

Kang et al (36) retrospectively reviewed data from 9 head and neck patients, 7 of whom were immobilised using a 5-point thermoplastic mask (Orfit) with a standard headrest and 2 who were immobilised using a 3-point mask with standard head rest. All patients were treated with IMRT for 25-35 fractions. The masks of five patients had the eye region cut out and 1-3 alignment tattoos were also placed on the chest of all patients. After initial set-up, position verification was firstly corrected through 2D-2D (orthogonal kV radiographs-DRR) matching and then further translational corrections were detected using 3D-3D co-registration (kVCBCT). Bony anatomy was used for matching, primarily C2 vertebra.

The authors reported intrafractional errors of <3 mm and noted that CBCT was useful in the detection of rotational differences. However, 2D imaging was sufficient to reduce the set up error.

Absolute average values for 2D imaging were 1.3 ± 1.6 mm in the lateral direction, 2.0 ± 1.9 mm in the CC direction and 0.6 ±1.4 mm in the AP direction. Corresponding

absolute values when 3D imaging was used were: 0.5 ±1.0 mm, 0.4 ± 0.9 mm and 0.3 ± 0.7 mm.

Kassaee et al (37) reported on a prospective study of 10 patients who were treated with SRS or SRT for either a boost phase or re-irradiation for head and neck or base of skull lesions. Patients were immobilised using a modification of the non-invasive, relocatable Gill-Thomas Cosman (GTC) head frame. Daily CT images were acquired for position verification and total systematic displacement was recorded at 0.8 mm.

Velec et al (38) reported on 20 patients who were randomised to either a standard thermoplastic mask (n=11) or a skin-sparing mask, modified with regions 'cut out' on the lower neck (n=9). Stability was checked at the bridge of the nose, ears and mandible. Patients were treated with an IMRT technique and daily CBCTs were acquired for position verification. An automated bony registration algorithm was used with specified anatomy in the clip box or a user-defined registration volume. Results between the two masks were similar, with no significant variation in either intrafraction or interfraction displacements observed and are given in Table 11.

Ahn et al (39) studied 23 patients with various head and neck primary lesions who were immobilised with a three point thermoplastic mask and a shoulder depression system. CT slices of 2.5 mm were acquired and position verification was through repeat CT scans at fractions 11, 22 and 33. Anatomy used in position verification included checking coordinates at various points such as skull base foramina, cervical spine and mandible, as well as the cochleae bilaterally, incisive foramen, mental foramina bilaterally, odontoid process, transverse foramina of C1-C7 and the midpoint of the posterior-most extension of the spinous process. Overall, the results indicated that improved immobilisation than the system described above, was required AP displacements ranged from a mean of -1.78 mm ± 2.68 mm (-9.30 mm to 3.00 mm) at the mandible to 0.02 mm ± 0.85 mm (-2.05 mm to 2.00 mm) when measured at the midpoint of the transverse foramen of T1. Craniocaudal shifts ranged from 1.86 mm ± 4.03 mm (-5.00 mm -20.00 mm) when measured at the mandible to 0.02 mm ±1.44 mm (-2.50 mm to +5.00 mm) when measured at C2. Lateral shifts were recorded as -1.18 mm ± 4.37 mm (-16.10 mm -9.20 mm) when recorded at the skull incisive foramen and -0.04 mm ± 1.62 mm (-5.45 mm -4.25 mm) when measured at C3. Changes in pitch ranged from -0.15° ± 4.55° (-11.07° to 9.28°) when measured at C2 up to 0.44° ± 2.45° (-4.74° -6.75°) when measured at C6. Yaw displacements ranged from 0.14° ± 3.09° (-7.93° -10.38°) when measured at C3 to 0.97° ± 5.57° (-11.30° to 21.43°) when measured at C2. The authors conclude that use of a bite-block fixation may improve the immobilisation of head and neck patients.

Bale et al (40) evaluated the adaptation of the Vogele-Bale-Hohner (VBH) head frame, which was originally designed for frameless stereotactic treatments to the requirements of 3D conformal external beam radiotherapy for head and neck cancer. Patient position was verified using a 3D navigation system (EasyGuide Neuro, Phillips) and a comparison was made between this and their standard head and neck fixation. Results were more positive for the VBH system showing a reduction in overall systematic displacements from 3.05 mm with the traditional system, whose baseplate was mobile, to 1.02 mm with the VBH system.

Fairclough-Tompa et al (41) report on 6 T1-T2 glottic patients who were randomised to a head and neck localiser, a head and neck localiser with a vac-lok bag or a Gill-Thomas-Cosman (GTC) frame as their immobilisation technique. Patients were treated with SRT and were imaged using portal imaging twice weekly. Both bony structures and patient external contour were used to verify position. Average displacements for the head and neck localiser alone were 3.0 mm - 6.2 mm (0.2 mm -14 mm). For the head and neck localiser and the vac lok, the average displacements were 2.0 mm - 3.0 mm and 0 mm - 5.2 mm and the GTC tolerance was recorded as < 1.5 mm.

Gilbeau et al (42) reported on prospective data from 30 patients, half of whom had brain tumours and half head and neck tumours. Within each group, there were three subdivisions and patients in each subdivision were assigned to one of a 3, 4 or 5-point indexed thermoplastic mask system. Patients were treated with a variety of 3DCRT beam arrangements, ranging from simple parallel-opposed lateral fields to multiple non-coplanar field arrangements. Portal imaging was performed weekly with matching of field edges as well as pre-defined bony anatomy including the mandible, clavicle and maxillary sinus. Shoulder fixation was statistically significantly worse with the 3-point fixation ($p<0.01$). Comparisons were made for the three devices at three different regions: the head, neck and shoulder levels. Overall deviations at the head level were reported as 0.7 mm for the 3-point, 0.9 mm for the 4-point and 1.0 mm for the 5-point. For the neck level, total displacement was 0.9 mm for the 3-point fixation and 1.0 mm for both the 4-point and 5-point. Deviations at the shoulder level were 3.0 mm for the 3-point, 0.8 mm for the 4-point and 1.2 mm for the 5-point.

Rotondo et al (43) reported on 21 head and neck cancer patients who were immobilised using either a 5-point thermoplastic mask (Type S) or with a head thermoplastic mask with a shoulder depression system (Accufix). Set-up times between the two systems were almost equivalent with patients treated with a 3DCRT technique. CT scans were acquired once per week during treatment and the odontoid process along with the styloid processes were used for the alignment of the upper neck, with the spinous process of C7 and the clavicles being used to align the anatomy of the lower neck region. Total random displacement for the Type S mask was 1.9 mm (SD) for the upper neck and 5.7 mm (SD) for the lower neck. Results for the Accufix system were 1.2 mm (SD) for the upper neck and 5.8 mm (SD) for the lower neck, indicating that a thermoplastic mask system that extends over the shoulders does not necessarily reduce random set up errors. Neubauer (44) also assessed shoulder position variation and its impact on IMRT and VMAT doses for 10 patients who were immobilised in 5-point thermoplastic masks and verified daily using CT-on-rails scans. These patients all had lower neck disease involvement with primary lesions in the nasopharynx, oropharynx, spine and mouth. Three of the patients were also simulated with wrist straps to pull the shoulders inferiorly and two of these were subsequently treated with these wrist straps in situ. Shoulder position variation was determined relative to the planning image. The average shoulder shifts observed were in the region of 2-6 mm. The majority (85%) of the shifts were less than 6 mm in magnitude, but all patients had at least one shift that was greater than 5

mm and 2% of shifts were greater than 10 mm. Most patients demonstrated a combination of systematic and random shifts, with larger shifts tending to be random. The patients for whom wrist straps were utilised to move the shoulders inferiorly did not show consistently smaller shifts than those who were treated without straps. The magnitude of the shoulder shifts did not increase with time, as may have been expected with patient weight loss as treatment progressed.

Linthout et al (45) reported on prospective data from 13 head and neck cancer patients who were immobilised with 3 types of five-point thermoplastic mask. These were the Orfit efficast with 2 mm thickness maxiperforation, the Orfit efficast with 1.6 mm thickness microperforation and the Orfitlight with 2.4 mm thickness microperforation. These patients were treated with either Arc therapy or dynamic MLC IMRT. Position verification was performed using the Novalis system where two stereoscopic kV images were acquired for comparison with DRRs of the same characteristics. Both 3D and 6D co-registration algorithms were used to measure translations and rotations for systematic errors and IR tracking and 6D fusion were used to measure random errors. Registration was performed aligning to the bony structures that were visible on both images. Systematic errors, as measured with 3D registration showed an overall mean of 0.5 mm in the AP direction, with the Orfit efficast with 1.6 mm performing best. However, for 6D fusion, the overall mean was -0.2 mm and Orfit efficast with 1.6 mm perforation performed the least favourably. For the craniocaudal direction, the Orfitlight yielded the greatest shift on both 3D and 6D fusion (-3.6 mm and -3.8 mm, respectively). Overall, the Orfit efficast with 2 mm perforation yielded the most consistent results when measuring translational shifts, either using 3D or 6D co-registration. Random translational shifts were similar, whether they were measured using IR tracking or 6D co-registration. The mean AP shift for all mask types on IR tracking was -0.1 mm and for 6D was -0.5 mm. The largest discrepancy on rotations was seen for pitch when using the Orfitlight system, with a mean pitch of 0.7° observed.

Table 12. Comparison of displacement results between immobilisation devices

Author	Year	Mask Type	Number of patients	Treatment Technique	Verification Method	Results/Set up errors measured Device A (mm)	Results/Set up errors measured Device B (mm)	Results/Set up errors measured Device C (mm)
Bentel	1995	Customised head support and masks	18	2D and 3DCRT	Portal imaging	Immobilisation masks improve patient repositioning when they are indexed to treatment couch.		
Hong	2005	Thermoplastic mask with maxillary bite tray with fiducials	20	3DCRT (n=10) and IMRT (n=10)	Weekly portal imaging Daily for those with the maxillary bite tray	Mean absolute error in any single dimenstion was 3.3 mm. With 6DF, a mean set up deviation of 6.9 mm (SD 3.6 mm) was found		
Sharp	2005	Head mask vs. head and shoulder mask by Poiscast	241	3DCRT	Portal images acquired twice. First, after treatment initiation and second after 4 weeks of treatment	No difference between the set up errors between groups, as measured by table positions		
Karger	2001	In-house cast of self-hardening bandages attached to a stereotactic frame.	4	Stereotactic RT	Orthogonal images acquired at each fraction	Recognised through repeated imaging that errors on the first fraction, if uncorrected, would be reproduced throughout remaining fractions		

Author	Year	Mask Type	Number of patients	Treatment Technique	Verification Method	Results/Set up errors measured Device A (mm)	Results/Set up errors measured Device B (mm)	Results/Set up errors measured Device C (mm)
Willner	1997	Bite-block fixation device and a semi-standardised head and neck support	29	Arc therapy	Fast film verification films acquired 4-6 times over treatment course	*Systematic errors:* AP: 2.7 CC: 2.5 Lateral: 3.1 Overall systematic displacement: 1.8 -2.2.	*Random errors:* Total random displacement: 1.9 - 2.1.	
McKernan	2007	POP-made rigid cast vs. Laser – made rigid cast	120	_	_	_		
Boda-Heggman	2006	Thermoplastic head mask vs. rigid cast mask	21	IMRT and 3DCRT with stereotactic set up	Daily CBCT	For intracranial region: thermoplastic mask AP: 1.54 ± 2.77 CC: 2.3 ± 2.33 Lateral: -0.2 ±2.27	For intracranial region: rigid cast mask AP: 0.05 ± 1.7 CC: 0.83 ± 2.3 Lateral: 0.39 ±1.75	
Donato	2006	3-point rigid mask (Uvex) vs. thermoplastic mask (Ultraplast)	20	3DCRT	Daily EPIs of right lateral only	*Systematic errors* (Uvex) AP: 2.6 CC: 1.6 Pitch: 1.3° (SD) *Random errors:* AP: 1.9 CC: 3.8 Pitch: 1.8° (SD)	*Systematic errors* (Ultraplast) AP: 1.9 CC: 1.8 Pitch: 1.6° (SD) *Random errors:* AP: 2.3 CC: 2.2 Pitch: 2.1° (SD)	

Author	Year	Mask Type	Number of patients	Treatment Technique	Verification Method	Results/Set up errors measured Device A (mm)	Results/Set up errors measured Device B (mm)	Results/Set up errors measured Device C (mm)
Humphreys	2005	4-point rigid mask (Cabulite)	20	IMRT	Orthogonal EPIS acquired daily for week 1 and weekly thereafter	*Systematic errors* (Cabulite) AP: 0.02 CC: 0.7 Lateral: 0.9 Pitch: 0.5° Yaw: 0.2°	*Random errors (SD)* (Cabulite) AP: ±0.7 CC: ±0.6 Lateral: ±0.4 Pitch: ±0.3° Yaw: ±0.2°	
Kang	2011	3 and 5 point thermoplastic masks	9	IMRT	Weekly 2 D (kV) and 3D (CBCT) imaging. 2nd CBCT taken after RT to assess intrafraction motion	Overall 2D translational errors reported as 3.5 mm but were > 5mm for 30% of imaging days. 3D imaging resulted in a small incremental adjustment of 0.8 mm.		
Kassaee	2003	Modification of Gill-Thomas Cosman frame (GTC)	10	Stereotactic RS or RT	Daily CT imaging	Total systematic displacement: 0.8		

Author	Year	Mask Type	Number of patients	Treatment Technique	Verification Method	Results/Set up errors measured Device A (mm)	Results/Set up errors measured Device B (mm)	Results/Set up errors measured Device C (mm)
Velec	2010	Standard thermoplastic masks (SM) vs. modified skin-sparing masks with low-neck cut-outs (SSM)	20	IMRT	Daily CBCT	*Initial Interfraction error* (SM) AP: 1.6 CC: 1.5 Lateral: 1.5 Roll: 1.1° Pitch: 0.9° Yaw: 0.9° *Residual Interfraction error:* AP: 1.3 CC: 1.3 Lateral: 1.3 Roll: 0.8° Yaw: 0.8° Pitch: 0.8° *Residual intrafraction error:* AP: 0.8 CC: 0.7 Lateral: 0.8 Roll: 0.7° Pitch: 0.7° Yaw: 0.6°	*Initial Interfraction error (SSM)* AP: 1.6 CC: 2.0 Lateral: 1.3 Roll: 0.8° Pitch: 0.8° Yaw: 0.8° *Residual Interfraction error:* AP: 1.3 CC: 1.5 Lateral: 1.2 Roll: 0.8° Yaw: 0.8° Pitch: 0.8° *Residual intrafraction error:* AP: 0.8 CC: 0.8 Lateral: 0.8 Roll: 0.7° Pitch: 0.6° Yaw: 0.8°	

Author	Year	Mask Type	Number of patients	Treatment Technique	Verification Method	Results/Set up errors measured Device A (mm)	Results/Set up errors measured Device B (mm)	Results/Set up errors measured Device C (mm)
Ahn	2008	Short face mask with shoulder depression system	23	IMRT	CT scans at fractions 11,22 and 33.	No correlation between positional variation and fraction number. Semi-independent rotational and translation movement of the skull in relation to the lower cervical spine was shown. Positioning variability was largest in the mandible and lower cervical spine.		
Bale	1998	Adapted Vogele-Bale Hohner head holder (VBH) vs. standard mask and neck rest		3DCRT	3D navigation system (Easy-guide Neuro from Phillips Medical Systems)	Head and neck mask: Total systematic displacement: 3.05	VBH: Total systematic displacement: 1.02	
Fairclough-Tompa	2001	Head and neck localizer (HNL) vs. head and neck localizer and vac-lok (HNL-VK) vs. Gill-Thomas Cosman (GTC)	6	Stereotactic RT	Portal imaging twice per week	HNL: Average set up error: 3.0 -6.2 Range: 0.2-14	HNL-VK: Average set up errors: 2.0 -3.0 Range: 0-5.2	GTC: Tolerance < 1.5

Author	Year	Mask Type	Number of patients	Treatment Technique	Verification Method	Results/Set up errors measured Device A (mm)	Results/Set up errors measured Device B (mm)	Results/Set up errors measured Device C (mm)
Gilbeau	2001	3,4 and 5 point thermoplastic masks	30	2D and 3DCRT	Weekly portal imaging	Shoulder fixation was significantly worse with 3 point fixation. 3-point mask: Head level errors: 3.1 ± 1.0 Neck Level: 2.3 ± 0.8 Shoulder level: 2.5 ± 1.2.	4-point mask: Head level: 2.4 ± 0.8. Neck Level: 1.7 ± 1.0 Shoulder Level: 3.7 ± 1.1.	5-point mask: Head Level: 2.4 ± 0.9 Neck Level: 2.2 ±1.0 Shoulder Level: 2.8 ± 1.1.
Rotondo	2008	5 point thermoplastic mask (Type S) versus thermoplasrtic head mask with shoulder depression system (Accufix)	21	3DCRT	CT images	*Random errors at upper landmark:* (Type S) AP: 1.8 CC: 2.5 Lateral: 1.7 *Random errors at lower landmark:* (Type S) AP: 6.4 CC: 5.8 Lateral: 4.9	*Random errors at upper landmark* (Accufix) AP: 2.0 CC: 1.7 Lateral: 1.3 *Random errors at lower landmark:* (Accufix) AP: 6.0 CC: 4.6 Lateral: 6.3	
Neubauer	2012	5-point thermoplastic mask from ORFIT	10	IMRT and VMAT	Daily CT on rails imaging	Average shoulder motion: 2-6 mm in each direction. 85 % observed shifts were < 6mm and 2% > 10 mm. Largest shoulder shifts in AP and CC directions.		

Author	Year	Mask Type	Number of patients	Treatment Technique	Verification Method	Results/Set up errors measured Device A (mm)	Results/Set up errors measured Device B (mm)	Results/Set up errors measured Device C (mm)
Linthout	2006	3 types of 5-point thermoplastic mask	13	Arc Therapy and dynamic MLC IMRT	Stereoscopic kV imaging using 3D and 6D fusion	*Systematic errors 6D fusion* (Orfit Efficast 2mm perforation) AP: 0 CC: 0.6 Lateral: 0.3 Roll: -0.2° Pitch: -0.5° Yaw: 0.7° *Random errors:* AP:-0.3 CC: 0.3 Lateral: 0 Roll: 0.1° Pitch: -0.2° Yaw: -1.0°	*Systematic errors 6D fusion* (Orfit efficast 1.6mm perforation) AP:-1.3 CC: 2.2 Lateral: 0.5 Roll: -0.2° Pitch: 0.4° Yaw: 0.7° *Random errors:* AP: -0.1 CC: 0 Lateral: 0.5 Roll: 0 Pitch: -0.3° Yaw: -0.4°	*Systematic errors 6D Fusion* (Orfitlightl, 2.4 mm perforation) AP: 0.5 CC: -3.8 Lateral: 1.8 Roll: -0.7° Pitch: -1.8° Yaw: 0.9° *Random errors:* AP: -1.3 CC: 1.0 Lateral: -0.3 Roll: 0 Pitch: 0.7° Yaw: -0.4°

4.1.2 Customised Neck-rests for HN RT

There has been substantial research interest in the evaluation of neck supports for many years. Bentel (46) prospectively analysed a head and neck support system as far back as 1995. This study compared the immobilisation of 18 patients with various diagnoses of head and neck cancer using a customised head support compared to the previous six standard head supports used. Patients were treated with a 2D technique. Measurements were made at various points between the treatment couch and the head support in the anterior-posterior and superior-inferior directions in order to ascertain which head support system was superior. The customised support was deemed to increase set-up accuracy. Similarly Marsh (47) retrospectively analysed the efficacy of a custom-made foam cradle to immobilise the head and shoulders, coupled with a thermoplastic mask in 20 patients. Portal films were compared to DRRs using a graphical alignment tool. The location of the isocentre, as well as in-plane translations and rotations were analysed. It was concluded that this method of immobilisation was reasonably accurate, easy to use and cost efficient.

Li et al (48) prospectively analysed 21 patients with head and neck cancer who were immobilised for radiation therapy using either a thermoplastic mask with a standard headrest (n=10) or a thermoplastic mask with a vacuum bag (n=11). Patients were treated with IMRT and had weekly imaging of either 2D kV-kV or CBCT. One of the most prominent landmarks used for matching was C2. Overall, set up errors, as noted on 2D imaging, were 0.5 mm in the AP direction, 0.6 mm in the CC direction and 0.6 mm in the lateral direction. Interestingly, these increased to 1.6 mm, 1.5 mm and 1.3 mm respectively, when analysed in 3D using CBCT. Further analysis illustrated that set up errors with the standard head rest were smaller in all directions than those with the customised head rest, when analysed on CBCT. The AP error reduced from 1.8 mm to 1.4 mm, the CC error from 1.9 mm to 1.4 mm and the lateral reduction was more modest, 1.2 mm to 1.1 mm. When analysed on 2D kV imaging, the AP improvement with the standard head-rest was from 1.6 mm to 0.8 mm but was the same as the customised neck rest in the lateral direction and slightly inferior (by 0.1mm) in the CC direction. This study illustrates the impact not only of patient positioning and immobilisation on set-up error but also the impact of the image guidance method in assessing these inaccuracies.

Houweling et al (49) prospectively compared set-up deviations in 22 head and neck cancer patients immobilized with either a customised head support or a standard head support. On-set verification was by weekly CBCTs, pre and post-treatment. Five alignment boxes were defined to determine the inter and intra-fraction displacements. These alignment boxes were: a general head and neck area, skull, mandible, C1-C3 vertebrae and C4-C6 vertebrae. It was noted that both the inter and intra-fraction errors of the translations and rotations were reduced significantly by using the customised head support. The largest reductions were observed in the neck region. For the deformation between the C1–C3 region and the skull, the systematic error of the translation along the AP-axis reduced from 2.7 mm with the standard head support to 1.1 mm using the individual head support. Overall, improvement in immobilisation using an individual head support reduced the

systematic and random errors of these displacements and deformations and the reproducibility and stability of patient positioning were improved.

Prisciandaro et al (50) retrospectively reviewed the set-up errors of 26 patients who were treated with either the UON head and neck immobilisation mask with four standard head rests from Nuclear Associates or with the Type S head, neck and shoulder immobilisation system with customised head supports from MedTec. Patients were verified with EPIs using the skull, C1 and C4 spinous processes and /or the clavicle as anatomy for bony matching. Systematic errors for the UON system were marginally more favourable than for the Type S system in the AP direction (range of -0.2 to 0.6 mm and -0.4 to 0.8 mm) but the Type S system was more favourable in the CC and lateral directions than the UON system (-0.2 to 1.1 mm compared to -1.1 mm to 1.0 mm and -0.3 mm to -0.2 mm compared to -1.2 mm to -0.8 mm, respectively). However, for random errors, the Type S system was more favourable in reducing deviations in all directions.

Van Lin (51) et al also reported on 36 patients who were immobilised either with a standard neck support (n=17) or with a customised head support (n=19). Position verification was through an offline SAL protocol with EPIs using bony match structures such as the skull base, body and spinous process of C2 and other visible vertebral bodies, nasal septum and maxillary sinus. The systematic variation was reduced with the customised head support in the CC and AP directions from 1.2 mm to 0.8 mm and 1.4 mm to 0.8 mm, respectively. The systematic error in the lateral direction increased from 0.8 mm to 1.1 mm with the customised head support. All random errors were improved upon using the customised head supports, although the improvement in the lateral direction was modest (from 1.9 mm to 1.7 mm). Improvements from 1.5 mm to 1.1 mm were seen in the CC and AP directions. Both systematic and random errors reported here were after the application of an offline correction protocol.

From our survey results, a combination of standard and customised neck rests are currently used throughout Europe with standard neck rests most commonly used for 3DCRT techniques and a combination of standard and customised for modulated techniques such as IMRT and VMAT.

4.1.3 Skin-sparing effect of thermoplastic masks

Fiorino et al (52) measured the skin sparing effect of 2 mm and 3.2 mm layers of Orfit, 2.55 mm layer of Posicast and 2.4 mm and 3.2 mm layers of Primod. It was concluded that both the mask thickness and perforation of the thermoplastic layers are important in the skin-sparing effect. These were measured in vitro as, in clinical situations, it is not possible to accurately perform reproducible measurements as the thickness and perforation are variable between masks from different vendors and even at different points on the same mask from any one vendor.

4.1.4 Impact of weight loss or tumour shrinkage during RT

Ezzel et al (53) reported on 8 patients with various primary lesions in the head and neck, who were treated with IMRT and who had repeat CT scans during the course

of treatment due to weight loss or tumour shrinkage, as observed by the clinician. Some patients had to have their immobilisation device re-made due to weight loss. The average time between scans was 28 days. In order to match the two CT datasets, the superior tips of the right and left temperomandibular joints, the occipital crest and the cervical vertebrae were used. The mean translational shifts between the two CT datasets were 2.5 mm laterally, 2.9 mm in the AP direction and 2.7 mm in the CC direction. Rotational shifts were in the range of 0.8°-1.8°. The authors concluded that uncorrected rotational shifts are particularly important in patients with weight loss and/or tumour shrinkage and that in the absence of six degrees of freedom corrections, rotational shifts can be misinterpreted as translational shifts.

4.2 Methods of Position Verification

Kang et al (54) analysed the data of 9 patients with locally advanced head and neck cancer. Patients were immobilised in either a 5-point thermoplastic mask (n=7) or a 3-point thermoplastic mask (n=2) and were treated with IMRT. Position verification was achieved using weekly kV imaging, manually matching on the cervical spine, in particular on C2, as well as weekly CBCTs. In order to assess intrafractional motion, a second CBCT was obtained post-treatment. An automated registration was then retrospectively applied using an automatic rigid body algorithm. In cases where there were large rotations observed, patients were re-positioned.

An average of the absolute values of the translational shifts of 3.5 ± 2.2mm was observed in the 3D length for the 2D-2D registration, however this was >5 mm for 30% of the imaging days. The addition of 3D imaging resulted in a small absolute incremental adjustment of 0.8 ± 1.5mm. The average rotational error was inferior to 2° with a range of 4°. The authors concluded that manual 2D registration reduces set-up errors and the addition of CBCT adds a slight improvement.

Sijtsema et al (55) analysed whether images of treatment fields were correlated with standard orthogonal fields and thus could potentially be imaged instead of orthogonal fields for position verification. Two different 3DCRT treatment techniques, with varying oblique fields were investigated. For the first oblique set-up, patients were immobilised in a 5-point thermoplastic mask and for the second oblique set-up; patients were immobilised in a 3-point thermoplastic mask. AP and lateral portal images as well as portal images of left and right oblique treatment fields were acquired. An offline SAL protocol was used. For the first oblique technique, a correlation between the orthogonal and oblique fields was observed and it was concluded that oblique field imaging could be used offline. For the second oblique technique, using a 3-point mask for immobilisation, it was concluded that orthogonal images only should be used. Difficulties in bony structure recognition using the oblique treatment beams, relative to orthogonal images were noted.

Ove et al (56) retrospectively reviewed 20 head and neck cancer patient datasets in order to quantify the set-up variation of the low neck in relation to the upper neck.

Patients were immobilised using a thermoplastic mask, coupled with a bite block to immobilise the mandible. One to two 2.5 mm shims were used to allow for mask shrinkage. Patients were treated with an IMRT technique and position verification was achieved using daily CTs acquired using the CT on rails in the treatment room. In general, CTs were matched to the bony anatomy of the upper neck at the level of C1 or C2. There was also a low neck point defined as the anterior-most portion of the cervical spine on the lowest CT slice on which the thyroid gland was visible bilaterally. The mean systematic shift of the lower neck relative to the upper neck was 3.08 mm in the AP direction. Mean random shifts relative to the upper neck were 3.9 mm in the AP direction, 2.6 mm in the CC direction and 3.3 mm laterally. The results suggested that larger planning margins should be used for the lower neck volume if it is located some distance from the region of fusion.

Giske et al (57) reported on their retrospective analysis of 45 patients who were treated with IMRT for oropharyngeal, laryngeal or locally advanced nasopharyngeal cancer. Patients were immobilised with a customised fixation device consisting of a scotch-cast mask and a vacuum mould. Additional tattoos were placed on both shoulders to ensure correct positioning of the shoulders in the mould. Oropharyngeal patients had a tongue depressor to increase the space between the tongue and the palate. The authors defined a number of local registration boxes (LRBs), which contained anatomic structures expected to show interfractional position variations. These included the skull base, the nose, C1-C2, mandible, C6, Larynx, T2 and right jugulum (the medial aspect of the right clavicle). This study illustrated that for these different anatomic sub-volumes, different movements are possible, determined both by the fixation of the patient and the range of motion of the various anatomic landmarks. The authors found that the skull base region was less susceptible to the anatomic changes caused by weight loss, whereas in the neck area, patient positioning is more affected by fat catabolism. It was also noted that, when using a scotch-cast mask, where no head support is present, the bending of the neck would be slightly different in all patients, depending on the length of the patient's neck. This study concluded that despite a sophisticated method of patient fixation, such as the scotch-cast mask, considerable deformations still occur in head and neck patients. However, in routine clinical practice, it can be advantageous to select a local registration box that provides the optimal correction vector for the specific location of the tumour, that is, an individual weighting of the relevant anatomic structures might be beneficial when performing registrations instead of selecting more general landmarks.

In a further attempt to increase set-up accuracy, Oita et al (58) prospectively evaluated the set-up of 8 patients with a diagnosis of pharyngeal cancer who were treated with a thermoplastic mask and customised head rest as well as a mouthpiece in which gold fiducials were implanted. Patients were treated with step and shoot IMRT and imaged daily using 2D kV-kV real time tracking. Time required to match fiducials was fewer than five minutes post-initial set-up. Comparison of manual matching versus matching with fiducials illustrated that translations were reduced from 1.2 mm to 0.2 mm in the AP direction, from 1.6 mm to 0.3 mm in the CC direction and from 1.8 mm to 0.2 mm in the lateral direction. However, rotations

remained the same between the two with roll reported at 2.2°, pitch at 3.3° and yaw at 2.5°. McKernan et al (59) reported on their retrospective audit, which yielded a mean systematic error improvement from 3.4 mm to 2.1 mm when the use of customised neck supports were introduced in their department. Position verification was achieved using EPIs.

4.3 Set-up errors in HN RT

4.3.1 Quantification of set-up errors

Schubert et al (60) reported on 30 patients who had a histologically proven malignancy of the head and neck region and who were treated with radiation therapy with a minimum of five fractions. Patients were immobilised in thermoplastic masks and sponge head rests. Slice thickness at CT was 2.5 mm. Patients were treated with helical Tomotherapy and had daily MVCT imaging. Both bony and soft tissue matching were performed. 1.2% of treatment fractions were shifted >10 mm 3D vector distance while 4.2% of fractions were observed as having rotations > 3°. Mean systematic errors in AP direction were -0.1 mm and 1.2 mm for the CC and lateral directions with a mean roll of 0.1° observed. Random errors of 1.9 mm for the AP and CC directions were observed, with a similar displacement of 1.8 mm observed laterally. Random roll was reported as 1.2°.

Johansen et al (61) retrospectively reviewed 34 head and neck patients who were receiving radiation therapy to a total dose of 66-68 Gy in 33-34 fractions. Patients receiving either primary chemoradiation or postoperative radiotherapy were considered. Patients were immobilised with customised vacuum cushions (VacFix) and full thermoplastic masks (Aquaplast) covering the shoulders. CBCTs were acquired on fractions 1, 2, 3 10 and 20 and both bony and soft tissue matches were performed using an automatic grey scale matching algorithm in a clip box. Correlations were observed between translational and rotational errors as well as between the set-up error at the start of treatment and by the tenth fraction. No correlation existed between the set up error, patient's weight, height or body mass index (BMI). A trend was observed in that random errors increased with increasing fraction number for translations in all directions. For example, for the AP direction, the random error at fractions 1-3 was 1.1 mm and this increased to 2.3 mm by fraction 10 and again to 2.6 mm by fraction 20. Similar increases were observed, albeit of differing magnitudes, in the CC and lateral directions. Random roll and yaw were reported as 0.7° for fractions 1-3 and as 0.5° for pitch. These were not reported for subsequent fractions.

Pehlivan et al (62) reported on 20 head and neck patients with tumours of the oropharynx, nasopharynx, paranasal sinuses, hard palate and hypopharynx. These patients were immobilised in a five-point Posicast mask on a Posifix carbon plate. The head was supported according to the neck position required and knee supports were also used. 3 mm slices were acquired at CT and patients were treated with an IMRT technique. Patients were imaged daily with EPIDs, which were matched to the patient contour. Total systematic displacement was recorded as 1.2 mm, with 0.93 mm recorded for the AP direction, 1.2 mm for the CC direction and 0.89 mm for the

lateral displacement. The largest random displacement reported was in the CC direction at 2.26 mm.

In 2007, Gupta et al (63) reported on 25 patients with head and neck tumours who were immobilised on a four-clamp baseplate with a customized thermoplastic mask and appropriate neck rest. Patients were treated with a 3DCRT approach and daily EPIDs were acquired for position verification purposes. Systematic errors in the AP, CC and lateral directions were recorded as 0.96 mm, 1.2 mm and 0.98 mm, respectively. For the same directions, random shifts were recorded as 1.94 mm, 2.48 mm and 1.97 mm, yielding a total random displacement of 3.84 mm.

Vaandering et al (64) retrospectively reviewed data from 75 head and neck patients who were immobilised using five point fixation masks (Sinmed). Patients were treated with helical tomotherapy. A comparison was made between daily MVCT imaging or imaging on alternate weeks versus imaging during the first five fractions. The time required for MVCT acquisition, co-registration and correction of detected deviations was 10 ± 2 minutes. The authors found that imaging only during the first five fractions lead to greater residual deviations than imaging on alternate weeks. This was especially evident in the AP direction. No correlation between weight loss and set up deviation was observed. Mean systematic shifts in the AP, CC and lateral directions were 1.3 mm, 1.0 mm and 0.2 mm respectively. A mean roll of 0.5° was noted. Random deviations were similar with shifts of 1.5 mm in the AP and CC directions noted as well as a lateral displacement of 1.4 mm and a roll of 0.6°.

Bertelsen et al (65) retrospectively reviewed data from 47 patients treated with radical intent for both head and neck cancer or brain tumours. Patients were immobilised with customised vacuum cushions (VacFix) and full thermoplastic masks (Aquaplast) that covered the shoulders. CT slices were acquired at 3mm intervals at planning. Four CBCT protocols were compared for differences in translations and rotations. The protocols compared CBCT acquisition on Days 1, 10 and 20 or Days 2, 10 and 20 or Days 3, 10 and 20 or finally, Days 1-3, 10 and 20. Bony and soft tissue matching were performed using an automatic grey scale matching algorithm in a defined clip box. There was no difference between the four protocols in terms of translational shifts or rotations. However, it was noted that the performance of the protocols increased when the action level was decreased in both the AP and CC directions.

4.3.2 Dosimetric impact of set-up errors in HN RT

In order to adhere to dose volume constraints and hence reproduce the clinically accepted treatment plan on a daily basis, accurate positioning and immobilisation processes must be adhered to and displacements inherent to the process of radiotherapy must be minimised through image guidance.

Neubauer et al (44) reported on 10 patients with head and neck primary lesions in the nasopharynx, oropharynx, oral cavity and cervical spine. Patients were immobilised in a 5-point thermoplastic mask by Orfit. Three patients were also simulated with wrist straps that pulled their shoulders inferiorly. Patients were treated with either IMRT or VMAT and position verification was achieved through daily CT

imaging, using CT on rails. Shoulder position was determined using the location of the head of humerus and neck position was verified using vertebrae C2-T3. Average shoulder motion was 2-6mm in each direction. 85% of observed shifts were < 6 mm and 2% were > 10 mm. Interestingly, patients who had been simulated with wrist straps did not show consistently smaller shifts. Largest shoulder displacements were observed in the AP and CC directions. For both IMRT and VMAT, superior shoulder shifts resulted in the greatest loss of target coverage and this was comparable between the two techniques. For example, a 5 mm superior shift illustrated coverage losses of 2-24 cm^3 at the 100% isodose level while a more dramatic 15 mm superior shift could cause a coverage loss of more than 100cm^3 at the 100% isodose level and more than 40 cm^3, when considering the 95% isodose coverage. This was attributed to the fact that a superior shift brought the shoulder into a region where it had not been previously and therefore both the depth and beam attenuation to the target were changed. This was not 'evened out' by a subsequent inferior shift, as although the dose will be increased slightly, it will be to a different transverse section of the neck. For IMRT plans, an increase in brachial plexus dose was found for anterior shifts, but these were not observed for VMAT plans.

Siebers et al (66) described a retrospective dosimetric study in which 22 head and neck patient datasets had simulated systematic and random errors applied and the dosimetric consequences were analysed. All patients were immobilised in reinforced thermoplastic masks and were treated with the SIB-IMRT treatment technique. Random and systematic errors were firstly simulated separately and then together. It was found that in the absence of systematic errors, 3 mm random errors alone had little impact on the target coverage whereas systematic errors of 3 mm had a negative effect on target coverage, indicating the importance of correcting for the systematic error. This study indicated that GTV D98 was the parameter that was most sensitive to patient positional uncertainties and despite the adjacent tissues being enclosed by a somewhat lower CTV dose level, rather than a sharp dose gradient in the SIB-IMRT technique, the coverage of the GTV D98 was still compromised in the presence of systematic errors.

4.4 CTV-PTV Margins in HN RT

Yu et al (67) reported on the long-term comparison of loco-regional recurrence (LRR) patterns and toxicity profiles among 367 patients treated with IMRT for SCC HNC with the use of either 3 mm or 5 mm CTV to PTV margins in the presence of daily IGRT. 55% of patients were treated with definitive RT and 45% with post-operative RT. Patient immobilisation was a perforated thermoplastic mask supported on a Timo cushion (S-type, Med Tec) mounted on an indexable carbon fibre board and the head, neck and shoulders were immobilised. CT planning slice thickness was 3 mm. 103 patients were treated with an isotropic CTV-PTV expansion of 5 mm (Group 1) while the remaining 264 patients were treated using an isotropic expansion of 3 mm (Group 2). Median dose was 66 Gy. Daily IGRT was performed using either kV CBCT or MV fanbeam. Overall survival was 71 % (Group 1: 69% and Group 2: 72%). No significant difference was observed in LRR between the two groups. Similarly, there was no significant difference observed in toxicity between the two groups. However

gastrostomy dependence for group 1 was 10% at one year and 3% for group 2 (p=0.001). The incidence of oesophageal stricture was 14% for group 1 and 7 % for group 2 (p=0.01). This study illustrated the potential for the reduction in some late toxicity, while maintaining the same LRC.

Kapanen et al (68) reviewed the data of 80 HNC patients who were treated to 60-70 Gy and immobilised on a Candor head and neck plate with 5-point C-frame including a head cushion and a five-point thermoplastic mask. CT slices were acquired at 3 mm intervals. Patients were treated with a 7-field IMRT technique and were imaged for fractions 1-3 and then once weekly. If the set-up error was ≥3 mm in any direction, imaging was repeated on the subsequent fraction. If the average systematic set-up error was ≥3 mm in the first three fractions or thereafter in any successive two fractions, corrections were applied. Image matching was performed using bony anatomy matching. The bony landmarks were divided into the four most important sub-regions and the combined effect of rotation, mutual movement and shape changes of the bony landmarks were considered, instead of assuming a rigid target. Systematic set up errors of 1.1 mm in the AP direction, 1.3 mm in the CC direction and 0.7 mm in the lateral direction were recorded. Random errors recorded were 1.3 mm, 1.6 mm and 1.2 mm in the AP, CC and lateral directions, respectively. CTV-PTV margins required when accounting for motion in the bony landmarks were approximately twice as large than if a rigid target had been assumed. PTV margins were also dependent on the sub-regions of bony anatomy related to the target volume as well as the frequency of IGRT and whether early correction of systematic error had been applied. This study concluded that to retain 5 mm CTV-PTV margins, 2D daily online bony matching with an action level of 4 mm is required.

4.5 Frequency of IGRT in HN RT

A study by Simpson et al (69) randomly sampled 1600 radiation oncologists by internet, email and fax to investigate their use of IGRT, clinical applications and their future plans for its use. IGRT was defined as technologies used for set-up verification or tumour localisation during treatment. There were 1089 evaluable respondents and 393 responses were received, yielding a response rate of 36.1%. 93.5% were using IGRT and this reduced to 82.3% when MV portal imaging was excluded from the definition of IGRT. The majority rarely used IGRT in fewer than 25% of their patients or used it infrequently in 25-50% of their patients. Of those using IGRT, head and neck was the second most common site where IGRT was used in 74.2% of cases, after genitourinary patients at 91.1%. Volumetric imaging was used in 56.9% of head and neck cases. kV planar imaging and volumetric imaging were used to a similar extent (57.7% versus 58.8%), while MV planar imaging was the most frequently cited at 62.7%. In fact, the percentage of respondents using at least one or more of the three modalities was 89.4%. In the future, 71.4% of non-IGRT users planned to adopt its use in their clinics, while of those who did use IGRT, 59.1% planned to increase its use in the future.

CHAPTER 5: PROCEDURES AT DIFFERENT RADIATION THERAPY CENTRES

SUZANNE VAN BEEK NKI/AVL

Chemoradiation

Chemotherapy in oropharyngeal tumours with elective nodes consists of:

a Protocol RADPLAT intravenous: Cisplatinum once a week in week 1,4 and 7 of the radiotherapy treatment, irradiation occurs after 15.30 on the day of chemotherapy.

b Protocol RADPLAT low dose: daily Cisplatinum concurrent with the radiotherapy treatment for 5 weeks, starting on day one, with a time interval of 1-2 hours between chemotherapy and irradiation and only in combination with a DAHANCA radiation scheme.

c Protocol RADPLAT carboplatin: Carboplatin once weekly on each Monday for 7 weeks, starting on day one of the irradiation. There is no time relation between the chemotherapy and the irradiation treatment.

Positioning and immobilising the patient

Patients are positioned on the modified Posifix® headrest (MPH) (Civco Medical Solutions, Kalona, Iowa, USA), Figure 20A. The MPH is a standard Posifix® headrest, available in different curvatures (Figure 20B), in-house extended with extra supporting wedges for the comfortable positioning of the neck (Figure 1A). The mould room technicians select the MPH, which is used for that particular patient during the whole course of radiotherapy.

The patients are positioned with the head tilted backwards (Figure 20C) using a five point thermoplastic mask (Efficast®, Orfit Industries, Wijnegem, Belgium) and a knee support (Civco Medical Solutions, Kalona, Iowa, USA) for stability and comfort.

The personnel responsible for this procedure are specialised mould room technicians (not RTTs)

During therapy, patients are setup using localisation lines on the mask and skin to align the patient to the isocentre lasers. Subsequently, the table is shifted to align the patient to the planned treatment position and then a couch shift correction of our imaging protocol is performed.

The personnel responsible for this procedure are RTTs.

Image acquisition protocol

All patients receive a planning CT scan (Somatom Sensation Open, Siemens AG, Erlangen, Germany) of the (whole) cranium to the sternum (upper part) acquired with a voxel size of 0.8x0.8x3 mm^3.

The personnel responsible for this procedure are RTTs, specialised in image acquisition.

Treatment planning process

The radiation oncologist delineates the GTV/CTV + CTV lymph nodes. The RTT delineates the organs at risk and performs the expansions from CTV to PTV (CTV to PTV margin = 5 mm). A Volume Modulated Arc Therapy is used as a radiation technique. The radiation dose for oropharyngeal tumours is 35 x 2 Gy (70 Gy) in a DAHANCA scheme (5 fractions in week 1, and 6 fractions in weeks 2-6, with an overall treatment time of 6 instead of 7 weeks) or a Simulated Integrated Boost. The tumour receives 70 Gy and the elective lymph nodes 46 Gy.

RTTs, specialized in treatment planning responsible for the delineation of OAR and creating the treatment plan, while the radiation oncologist is responsible for the delineation of the CTVs, dose prescription and plan approval.

Image verification protocol

During treatment, the patients undergo off-line CBCT guided RT (Shrinking action level, action level α=5 mm, number of initial fractions Nmax=2). The CBCT scans (Elekta Synergy 4.2, Elekta Oncology Systems Ltd, Crawley, UK, augmented with in-house developed software) are acquired with an energy of 120 kV and an isocentre dose of about 1 cGy and reconstructed with a voxel size of 1x1x1mm^3.

The local setup errors are computed using mROIs registration[1-3] on 9 bony structures (cervical vertebrae 1 (C1), 3 (C3), 5 (C5) and 7 (C7), lower jaw, hyoid bone, larynx, skull and jugular notch) (Figure 21). Each ROI is locally rigidly registered from CBCT scan to the planning CT scan using Chamfer-Matching. The average of the local setup errors is used to perform the couch shift correction. RTTs are responsible for irradiation of the patient and for the acquisition of images. Image-specialist RTTs are responsible for the imaging protocols.

Procedure followed due to immobilisation device instability

Immobilisation devices are rarely adjusted. No adjustments are made due to weight loss. Stretching the mask on the linac is allowed only in a few specific scenarios. In some cases (but this is the exception, on average once in 3-4 months) new masks are made. As a result a new planning CT and a new treatment plan must be performed. The specialised mould room technicians are responsible for stretching the mask and the decision to make a new mask lies with the radiation oncologist.

Procedure followed when tumour shrinkage is observed

We follow our 'traffic light' protocol for this subject.

We inform the radiation oncologist if tumour shrinkage (≥ 1.0 cm, ≥2 cm or more) is seen on the CBCT scan. The radiation oncologist only requests a new planning CT and treatment plan if the tumour (CTV) is not in the PTV. The RTT and imaging specialist RTT are responsible for the 'traffic light' protocol and the decision to acquire a new planning CT remains with the radiation oncologist.

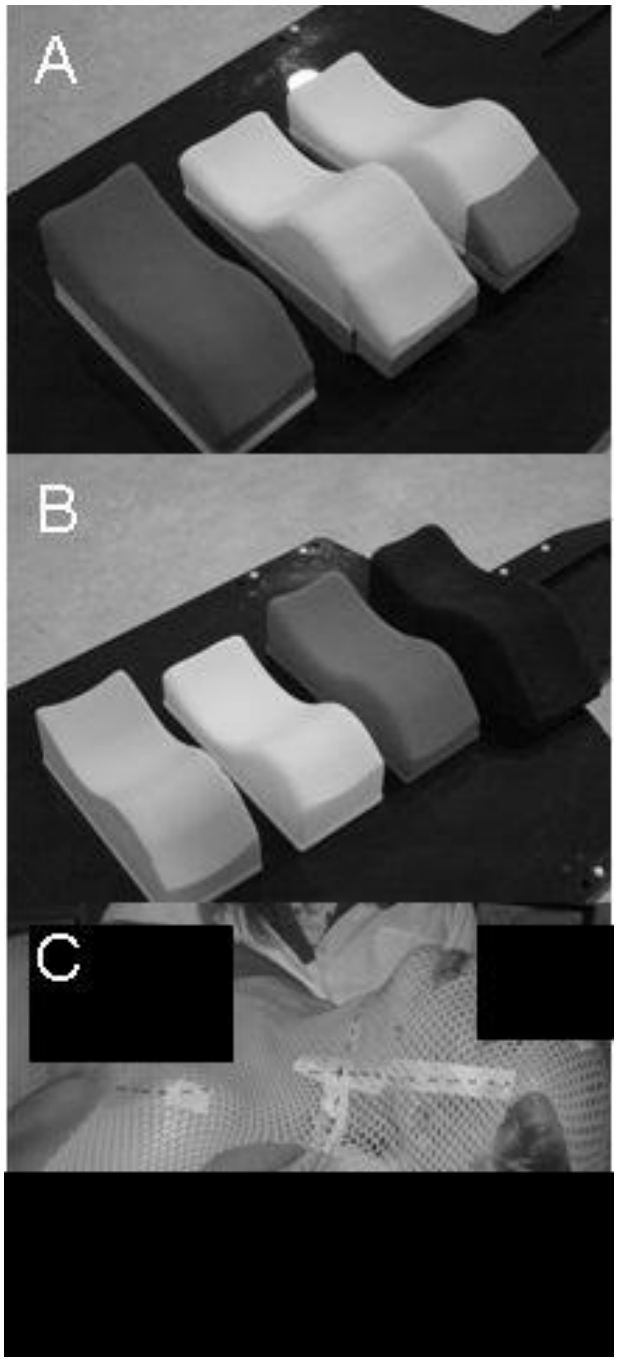

Figure 20. Positioning and Immbolisation equipment (NKI)

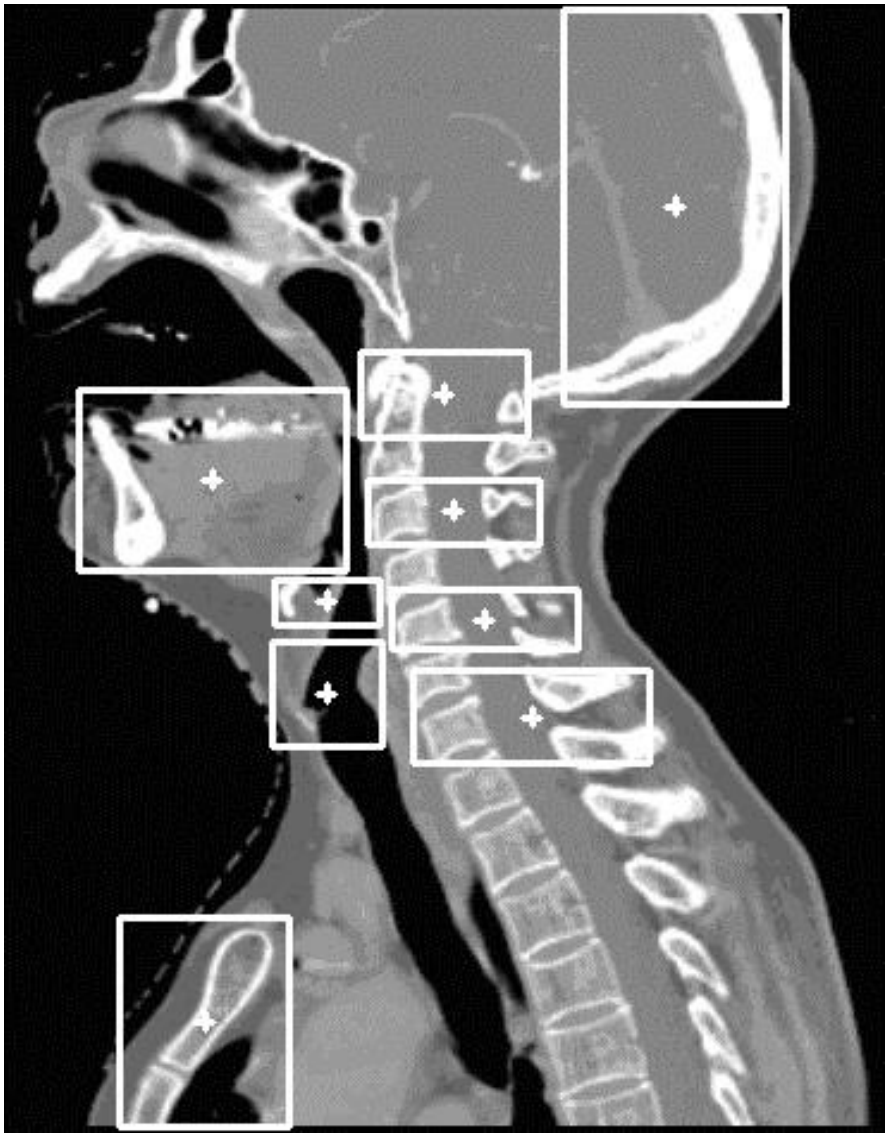

Figure 21. Regions of Interest (ROIs) for image matching. (NKI)

DANILO PASINI
"A. Gemelli" General Hospital - Catholic University of Rome
Radiotherapy department

Positioning and Immobilisation

For this kind of patient, we use a five point thermoplastic mask with a standard neck rest. We choose the neck rest that best fits the patient anatomy from the 6 available (A; B; C; D; E; F). Shoulder position is maintained with the mask itself.

RTTs are responsible for this step and they work in pairs in the CT simulator.

Image acquisition protocol

The acquisition protocol is stored on the CT scanner. The set of images must include all of the skull, from the vertex, to approximately five centimetres below the sterno-clavicular joint. Helical acquisition is with a pitch ≤ 1 and slice thickness is 2.5 millimetres. The RTTs are completely responsible for this step.

Treatment planning process

The treatment planning technique used is IMRT sliding window with seven static fields (6MV, MLC 120 leaves). We utilise a simultaneous integrated boost technique or two or three alternate plans considering, each time, the different PTVs. The PTV is delineated by the RO and, usually, the OARs are delineated by RTTs and/or Residents. The treatment plan is created and calculated by RTTs under the physicist supervision. Treatment planning is a team activity but the overall responsibility is that of the Radiation Oncologist.

Image verification protocol

The verification protocol used for the start images (before the first fraction) consists of acquiring orthogonal images 0, 90° and one angled treatment field (for checking the field shape and to include this printed image in the patient folder for documentation) all with double acquisition, small view and large view, both with MV than with kV, using the on-board imager (OBI), which is the elective equipment for this kind of treatment. After the start images we acquire only the orthogonal images, twice a week.

The verification of these images is off-line. No action is taken if the displacement is < 3 mm. If the shift is >3 mm after three set of images, we can determine if it is a systematic error (correction) or a random error. The procedure we follow for random errors depends on the magnitude of the error. The Radiation Oncologist can decide that an on line verification is required before each fraction or, for random shifts > 5-6 mm that a new mask and/or a new simulation is necessary.

The image acquisition is the responsibility of the RTTs, whereas the image checking is the responsibility of the Residents and Radiation Oncologists.

Procedure followed due to immobilisation device instability

Under normal conditions, after 30 Gy (about 16/17 fractions) we prepare for a replan. The patient goes back to the CT-Sim and the RTTs verify the mask fit and, if it is still suitable, acquire a CT set needed for the re-planning.

If the mask is no longer a good fit, at this stage or at any time during the period of therapy, we proceed with a new mask and then CT and create a new treatment plan for the remaining fractions. Usually these operations are the task of the RTT.

Procedure followed when tumour shrinkage is observed

A shrinkage of PTV or OAR volumes is normally detected during the replanning process as we do not routinely use CBCT for head and neck patients. This is currently under investigation in our department, coupled with the use of a robotic couch. The new treatment plan with related new delineation, takes these volume modifications into consideration. Evaluation of volume shrinkage is carried out by the Radiation Oncologist and is his/her responsibility.

MIRJAM MAST
RCWEST/MCH Westeinde, The Hague, The Netherlands

Positioning and Immobilisation

The initial patient positioning is performed on the CT-simulator. The patient lies in a neck rest with the chin in 'up' position; i.e. the neck-extension position. A standard neck rest is used, positioned on the head-neckboard of the Posifix® positioning system (Sinmed, Reeuwijk, The Netherlands). Adjustments can be made by adding extra supporting wedges for optimising patient comfort and in doing so optimising the reproducibility of the position of the patient. The mask type we use is, a five point Posicast mask that includes the shoulders in the mould. Upper body clothing has to be removed. The position of the patient is defined by the radiation oncologist, the radiation therapist (RTT) and the mouldroom technician.

Image acquisition protocol

For the CT scan (Brilliance CT Big Bore Oncolgy 16 slice, Philips, Eindhoven, The Netherlands), Visipaque 320 Intravenous (Iodine) contrast is used and the scan is acquired using 3mm slice thickness. The patient is scanned including orbits and clavicles. The T1-weighted MRI scan (Siemens Symphony, 1.5 T) is acquired using Gadolinium contrast. The RTT is responsible for the CT procedure and for patient positioning in the mask on the CT and MRI scanner. The MRI is operated by a radiographer.

Treatment Planning Process

The fusion of the CT and MRI images is performed by the RTT. The radiation oncologist delineates the Critical Organs (OARs) and the Clinical Target Volume (CTV) on the fused images, this target volume includes the tumour and the lymph nodes according to the determined diagnosis. After this an isotropic margin of 5 mm is applied around the CTV, yielding the Planning Target Volume (PTV).

A 7-field IMRT plan is used to treat the patient. We also include additional position verification images in the plan to perform an on-line position verification procedure and take the dose of the position verification images into account. The RTT makes the treatment plan, this treatment plan is approved by the radiation oncologist and checked by a medical physicist. The radiation oncologist is responsible for the treatment at all times.

The most frequently used scheme for primary radiotherapy is 70 Gy in 2 Gy fractions over 6 weeks, 6 fractions a week. We use a simultaneous integrated boost with a prescription of 54.25 Gy in 35 fractions of 1.55 for the elective PTV.

Image verification protocol

Patients are verified daily using on-line 3D position verification by means of two orthogonal exposures with a planar view EPID (6MV). No action level is used for correcting the positioning errors, all misalignments are corrected for. The match structures used are the spinous processes of C5-C7 and the posterior skull for the AP direction, the spinous processes of C2-C3 and the line of the posterior longitudinal ligament for the lateral direction.

We are currently investigating weekly CBCT to follow-up on the position of the Planning Target Volume and the Organs at Risk.

The complete procedure is performed by the RTT.

Procedure followed due to immobilisation device instability

If significant stability-loss is noticed a new mask is made and a new CT scan is acquired to make a new treatment plan. Furthermore, we are developing a protocolled manner of checking weight and stability during treatment and subsequent action (CT, planning) to replace the current ad-hoc action.

Procedure followed when tumour shrinkage is observed

We are developing a procedure of checking tumour shrinkage with a CBCT during treatment and deciding upon subsequent actions (CT, planning).

STEPHEN COYNE
Radiation Therapy Services Manager,
Radiotherapy Department, Galway University Hospital, Ireland

Positioning and Immobilisation

Prior to positioning and immobilisation, the patient's baseline body weight is measured in CT. The patient is positioned supine on a Silverman type head-rest with a 3 mm shim and immobilized with a five point Aquaplast mask. A shoulder retractor is used during mask construction. For oropharyngeal patients, a stable mouth position with the hard palate suitably elevated is required. This may necessitate the use of a mouthbite, in some cases. The CT RTTs are responsible for this step, while the use of a mouthbite is at the discretion of the radiation oncologist.

Image acquisition protocol

The patient is aligned anatomically straight and confirmed on a pilot scan. The patient is scanned from the vertex of the skull to the clavicles. The scan is acquired in 2.5 mm slices and the number of images, together with the DLP is noted on the CT records. The CT RTTs have responsibility for this acquisition.

Treatment Planning Process

Delineation of the following regions of interest is the responsibility of the RTTs in CT and is completed before exporting the CT data to the treatment planning system. These include: Spinal cord with PRV, primary disease, nodal levels I-V, parotid glands and mandible. Patients are planned with a 7-field IMRT technique, created by the RTTs in treatment planning.

Image verification protocol

An offline extended no action level (e-NAL) protocol is adhered to, with a tolerance level of 2 mm using kV EPIs.

Procedure followed due to immobilisation device instability

If the patient is on treatment and the immobilisation device is progressively becoming looser, e.g. due to weight loss, then separations and FSDs are measured. If the mask is still deemed to be immobilising the patient but it is likely that it will become compromised in the future, a new mask is constructed and the patient is replanned. The patient can continue treatment on the original mask in the interim.

Procedure followed when tumour shrinkage is observed

Tumour shrinkage is only observed if replanning is required, as we do not have cone beam CT capacity. If shrinkage has occurred, this is considered during the re-delineation of target volumes.

FILIPE MOURA
Hospital CUF Descobertas, Lisboa, Portugal.

Positioning and Immobilisation

The patient lies in the supine position on a carbon-fibre support for head rest and mask fixation. Depending on the patient anatomy and cervical lordosis limitation, the neck rest and angle devices are defined to best accommodate the entire posterior surface of the head and neck. It is important that the space between the neck support and body surface in any direction is minimal. The type of thermoplastic mask used is a 5-point fixation due to the elective irradiation of the lower neck nodes. No additional device is used to maintain the shoulder position. Anatomical points that are take in consideration include, the supracilliary arches, jugular notch of sternum, chin and mandible. Reference marks are placed on the mask with tape and permanent pen. A tattoo is made on the sagittal line on the upper thorax, immediately at the end of the thermoplastic mask. If the patient has undergone a tracheostomy, only a 3-point fixation mask is used. In this clinical situation, additional tattoos are placed on the shoulders at the same level as a reference mark on mask and at the same longitudinal position of the medial tattoo on the upper thorax.

Image acquisition protocol

The helical acquisition is made with an 8-slice CT, with a slice thickness of 2.5cm and pitch of 0.8. No intravenous (IV) contrast is used. 120 kV and 130mA are used to acquire the volumes of interest (VOI plus a margin to take into account beam divergence and dose calculation of irradiated volumes outside the therapeutic region. The CT Dose Index (CTDI) is normally around 10-12mGy/slice. The RTT is responsible for this procedure.

Treatment Planning Process

Virtual simulation (VS) software is used to fuse the CT image set with PET-CT and/or MRI and is performed when available and necessary. On the VS the radiation oncologist (RO) defines the planning reference point and delineates the target volumes and respective clinical and geometrical margins. The CT image set is then sent via DICOM RT to the TPS, where organs at risk (OARs) are delineated by a Radiation TherapisT. A 3DCRT, IMRT or VMAT technique is selected according to the shape and dimension of the PTV(s) and surrounding OARs. The treatment normally comprises 2 treatment phases with the usual dose prescription of 70 Gy in 2 Gy fractions. Elective nodes receive an average dose from 46 Gy to 50 Gy. Treatment planning is performed and evaluated by RTTs, verified by a Physicist and finally reviewed and approved by a Radiation Oncologist.

Image verification protocol

kV-CBCT image verification is used. The acquisition protocol for H&N is performed with near half gantry rotation, with a small field of view (FOV) and low dose protocol. Typical CTDI is 1-2 mGy which uses 100kV and 36mAs with ~360 frames.

An $eNAL_{average}$ protocol is applied according to the following:

The first 3 first fractions are corrected online (online correction) and the mean values of the first 3 fractions online are applied on the 4th fraction.

The frequency of verification periodicity varies between patients and is a result of the individual variation of the patient, based on the first 3 fractions, relative to the population variability. For example, if an individual patient standard deviation (x,y,z) based on the first 3 fractions, is less than ~1.5mm (population random error-mean of individual SDs) verification is scheduled on a weekly basis. For the treatment course after the 4th fraction, applying the $eNAL_{average}$ protocol, the tolerance applied is ~2mm (2SD of population systematic error).

Rotation tolerance is 2°. If rotations between 2-3° are observed, a correction is applied and a new verification is scheduled for the subsequent fraction. If rotations are >3° and/or deviations > 2mm, the patient is repositioned and immobilized and re-verified. The RTT is responsible for these procedures.

Procedure followed due to immobilisation device instability

When progressive or sudden changes of device stability are detected during the positioning and immobilisation procedure, it is determined to what extend it should be corrected. Visual inspection of the mask and neck rest are performed. If the mask is to tight due to oedema, for example, it should be reported to the Radiation Oncologist. A new mask, new CT and new plan are constructed. If the mask is too loose due to weight loss or tumour shrinkage, a daily kV-CBCT is acquired to determine the location of the critical structures. If major changes are detected, usually between 5-10 mm, it should be reported to the Radiation Oncologist, RO who will define if and when replanning is necessary.

Procedure followed when tumour shrinkage is observed

RTTs make a visual judgement using the kV-CBCT 3D matching system tools to measure the amount of shrinkage. If there is a significant variation it should be reviewed by the physician. If agreed by the Radiation Oncologist, CT planning is then performed to provide the study set necessary for image registration, dose calculation and summation. A new mask and setup reference points must be created to ensure maximum accuracy and precision for the remaining treatment.

PAUL BIJDEKERKE
Department of Radiotherapy,
Univeritair Ziekenhuis, Brussels, Belgium.

Positioning and Immobilisation

Before CT planning, patients are invited to come to the simulator to make a 5- point mask of the head and shoulders for immobilisation (5-point hybrid head and neck mask by Orfit). After informing the patient of the procedure, the patient is placed on the simulator table (SLS simulator Philips). In all cases the patient support system is based on the AIO-SolutionTM (ORFIT Industries, Wijnegem, Belgium). This is the AIO base plate, low-density head and neck supports (Numbers 1 to 6), thin soft mattress, knee cushion and a feet cushion, separating the legs. The patient is aligned on the table using the projection of the longitudinal laser. The laser line must run through the middle of the nose, chin, jugular notch, sternum, pubis and feet cushion. Subsequently the mask is shaped around the head and shoulders.

Image acquisition protocol

The projection of the lasers is drawn (in the shape of a cross) on the mask; middle of the chin (lateral), approximately 1 cm under the upper lip (longitudinal) and approximately at the level of external auditory canal (height). External marks (thin lead wires) are placed on the drawings to indicate the isocentre on the CT images. The image acquisition (3mm slices, head first supine, FOV 500 mm) is completed on the CT scanner (Siemens big bore) at the Radiology department.

Treatment Planning Process

The technique used is an inversely planned simultaneous integrated boost (SIB), using TomoTherapy. The Clinical Target Volume (CTV) comprises the GTV with a 5 mm margin and this is expanded by 3 mm to give the Planning Target Volume (PTV). The goal is to irradiate the tumor (GTV – PTV) to the prescribed dose. At least 95% of the prescribed dose must be given to at least 95% of the target volume. Dose reduction is required on normal tissue such as salivary glands and spinal cord without compromising target coverage. 30 fractions of 2.35 Gy is delivered to the primary tumor and the pathological lymph nodes, yielding a total dose of 70.50 Gy. 30 fractions of 1.80 Gy are also planned to the regional lymph node areas, giving a total dose of 54 Gy.

Image verification protocol

Patients are treated on TomoTherapy (Accuray). Prior to every treatment, all patients receive an MV-CT scan. The length of the area of interest in the cranio-caudal direction to be scanned differs from patient to patient depending on the size of the PTV. At least the length of 3 vertebrae has to be scanned if the PTV is too small. A slice width of 0.6 cm is chosen as a standard for imaging.

The co-registration of the images is performed by two RTTs and at the start of treatment and once a week the RTT carries out the registration. Comments are then exchanged if needed. Points of particular attention for the co-registration are noted in the personal radiation file. Special attention is paid to the dose distribution of the PTV, spinal cord and glands.

Procedure followed when tumour shrinkage is observed

Advice from the physician and physicist is requested if there are any discrepancies or problems, e.g. loss of weight, tumor shrinkage or the 5-point mask becomes too tight.

CHAPTER 6: GUIDELINES FOR POSITIONING, IMMOBILISATION AND VERIFICATION IN HN RT

1 Positioning prior to thermoplastic mask construction

The aim of positioning and immobilisation should be to maximise patient comfort and reproducibility, and hence treatment accuracy throughout the course of treatment. Head and neck cancer patients may be positioned and immobilised in dedicated mould rooms or, more frequently, in the CT room. In either instance, it is a pre-requisite that the same laser alignment system and couch is present as at the linear accelerator.

1.1 Following departmental patient identification procedures, the patient should be brought to a designated patient information area.

1.2 A full and detailed explanation of the procedure should be given to the patient by an RTT.

1.3 During the consultation, the importance of remaining still and breathing normally throughout the procedure should be stressed.

1.4 Other aspects related to both the safety and efficacy of the procedure should be discussed with the patient including the likely mask temperature, and how the patient can alert the RTTs if they are having difficulty during the procedure.

1.5 The patient should be asked to remove all clothing from the waist up. Any dentures, hearing aids, toupees and tongue piercings must also be removed. The patient should be provided with a gown, which can be removed, as the procedure commences.

1.6 The patient should be positioned on the treatment couch, following their natural position in as comfortable and reproducible a position as possible. The saggital laser should be used to ensure straightness, checking that it bisects the nasal septum, sternal notch, xiphisternum and symphysis pubis as much as is possible. This aids in the minimisation of rotations.

1.7 All immobilisation devices must be indexed or fixed to the couch, to minimise rotational and translational errors. Neck rests should provide adequate support for the head and neck and no gaps should be present underneath the head of the patient nor at the top of the neck rest.

1.8 In the case of inadequate support of the head and neck by conventional neck rests, the position can be adapted by adding 'wedges' or using individual, customised neck rests, or a combination of both. Selection of 'wedges' underneath the neck rest should be based on the required position of the neck for treatment. The RTT should be aware of the diagnosis of the patient and the likely beam arrangement when selecting the most appropriate neck position, which is usually neutral or extended in

head and neck cases. Care should be taken to ensure that selected neck rests are of good quality and fit for purpose as differences in neck rests can result in discrepancies in positioning from pre-treatment to treatment areas (Figure 22).

Figure 22. Quality Assurance of neck rests

1.9 Any additional supports required for the procedure, such as knee rests or shoulder retractors should be indexed to the couch.

Figure 23. Non-indexed supports should be avoided

1.10 Depending on the site to be treated in the head and neck, the patient may require a mouth bite or customised stent. These may be constructed either in the radiotherapy department or by a specialist dental centre. If required, the mouth bite or stent should be in situ prior to construction of the thermoplastic mask. It is preferable for patients to be given time to grow accustomed to the mouth bite or stent, if possible, prior to making the mask.

1.11 Documentation of the fixed positions of all immobilisation devices should be performed by one RTT and checked by a second. Careful documentation of specific devices for the patient should be made, for example, clear annotation of mouth bites or stents.

1.12 The mask selection should be made according to the institution protocol for that specific sub site. According to the treatment site and disease extension, masks should be of 3 or more fixation points. If treating the low neck, a 4 or 5-point mask is recommended. If a 3-point mask is used, a device to maintain shoulder position, such as a retractor, is mandatory.

1.13 It may be necessary to cover the hair with cotton-type material and to ensure that the patient's airway is not compromised during the procedure. This may necessitate enlarging the gap for the nasal and mouth areas slightly. For post-operative patients with tracheostomies in situ, care should be taken to avoid airway obstruction. This will necessitate placing petroleum-based gauze over the stoma, which will not obstruct breathing, as well as making an appropriate sized gap in the material to clear the tracheostomy site.

2 Construction of thermoplastic mask

2.1 The patient should be positioned as outlined in 1.6 above prior to commencing the construction of the mask.

2.2 If using a water bath, the manufacturer's guidelines on water bath temperature should be adhered to, as should the length of time required for hardening of the mask.

2.3 The material should be placed in the water bath for the stated period of time, removed from the water bath and excess moisture should be drained. The temperature of the material must be checked before placing on the patient's skin.

2.4 If using an 'oven' to heat the material, it should be heated to the appropriate temperature and the material checked before placing on the patient's skin.

2.5 The material should be draped over the head and neck of the patient. For correct construction of a four or five point thermoplastic mask, three RTTs must be involved in the process. One RTT should be at the superior aspect

of the patient and one on either side. If constructing a 3-point mask, two RTTs are required.

2.6 RTTs must work quickly and accurately to mould the material closely to the patient's skin, ensuring that there are no gaps and that the neck position remains as required throughout the moulding procedure. This must be completed within 1-2 minutes, as the hardening process will then commence.

2.7 Specific attention should be given to the forehead, bridge of nose, chin and shoulders to ensure that the mask will provide adequate immobilisation of the patient. It is the responsibility of the staff member at the superior aspect of the patient to ensure that the head is held still in position, to minimise rotations.

2.8 The material should be allowed to harden for the specified length of time as per the manufacturer's recommendations. This can be anything from 5-15 minutes, depending on material type. You can reduce the cooling time with towel from the fridge, cold gel pads or use a cold hair dryer. The cooling process can also be completed by removing the mask and submerging in cold water before refitting to the patient.

2.9 The patient should be supported and reassured by the RTTs during this time period.

2.10 It is recommended that the mask be removed and refitted prior to commencement of CT scanning to ensure that the fit is correct and that the immobilisation provided by the mask is adequate. Specific attention should be paid to the most stable bony landmarks: forehead, bridge of nose, chin and good contact with the chest and shoulder area should be evident. This also allows the patient the opportunity to take a short break prior to the commencement of image acquisition, which is advisable.

Figure 24. Poor immobilisation at the nasal region

Figure 25. Good immobilisation of forehead, nose and chin

Figure 26. Poor immobilisation of the shoulder and upper thorax

Figure 27. Good immobilisation of the upper thorax

2.11 The procedure and patient position should be clearly documented by RTTs in the patient chart. For safety reasons, the patient name, type of neck rest and wedges, is used should always be documented on the patient mask.

3 CT procedure

3.1 All departmental procedures in relation to patient informed consent and identification should be adhered to prior to commencing the CT scanning procedure.

3.2 The patient diagnosis, prescription and required scanning margins should be known to the RTTs before commencing CT, so as to adhere to the ALARA principle. Scanning margins as per local standard operating procedures (SOPs) should be adhered to.

3.3 If contrast is to be used, the RTTs must screen the patient for potential anaphylaxis as per departmental protocol, document this screening procedure and ensure that the emergency trolley is prepared and fully stocked. It is necessary to check the patient creatinine clearance prior to intravenous contrast administration. The RTT must ensure that the contrast is heated to 37 degrees Celsius to match the patient body temperature. According to national and local departmental policies, a radiation oncologist or other nominated clinician may need to be present during the cannulation and contrast administration procedures.

3.4 If wire marking of any nodal regions or post-operative surgical scars is required, this should be performed prior to patient immobilisation.

3.5 The patient should be (re)-positioned accurately on the treatment couch with the thermoplastic mask in situ. In cases where the mask has been constructed in the CT room, the patient will already be correctly positioned.

3.6 If bolus is planned for the patient's treatment, this should be in situ prior CT scanning so as to account for the actual bolus to be used at treatment in the dose calculations. This is preferable and more dosimetrically accurate than adding bolus during the treatment planning process and constructing it after the plan has been created. For head and neck cases, individual, customised bolus should be constructed.

3.7 Care should be taken to ensure that the treatment couch is set at an appropriate height so as to ensure that the immobilisation device is within the field of view (FOV). This is important, as the immobilisation device must be contoured, along with the targets and organs at risk, prior to beam modeling.

3.8 The correct scanning protocol for the head and neck should be selected as per departmental procedures.

3.9 The RTTs must ensure that both patient orientation and the orientation of the topogram or pilot scan are correctly entered at the CT console.

3.10 The RTTs should use the topogram or pilot scan to confirm the scanning borders that are required for the head and neck case. It is advisable to check orthogonal topograms and a single axial slice prior to the full scan to check for rotations.

3.11 It is recommended to use axial slice thickness of 3 mm or less for head and neck cases. This is to ensure sufficient anatomic detail for target and organ at risk delineation, minimising the partial volume effect, as well as adequate anatomic detail on digitally reconstructed radiographs (DRRs) from the treatment planning system (TPS), which will be used in treatment verification procedures.

3.12 The dose length product (DLP), number of axial slices and scan length should be documented in the patient chart. This is in line with the European Commission directive 97/43 (Euratom) on the recording of dose reference levels for imaging using ionising radiation.

3.13 Following the CT procedure, scan data can be exported to the TPS or virtual simulation software for delineation.

3.14 The patient can be removed from the scanner and the thermoplastic mask removed. If needed, a photograph of the patient position can be taken and added to the patient chart. If contrast has been administered, the departmental protocol in relation to observation should be adhered to prior to the patient leaving the department. As a minimum requirement, the patient must remain in the department for a further fifteen minutes.

4 Treatment Verification and delivery

General Principles:

4.1 The quality of positioning and immobilisation should be verified on a daily basis by visual inspection of positioning and immobilisation devices.

4.2 The patient weight should be monitored on a weekly basis as significant weight loss may ultimately necessitate a re-plan.

4.3 If the mask appears too loose or too tight, the RTT should evaluate the positioning and immobilisation devices, patient weight and volumes through portal imaging (2D) or cone beam CT (3D), as appropriate.

4.4 In the absence of 3D volumetric imaging capabilities, it is advisable to perform a new CT scan either between treatment phases or after a pre-defined number of fractions for simultaneous integrated boost techniques, as a check point for target volumes, OARs and external contour variations.

Methods of Image Verification: As seen in Chapter 2, there are many imaging modalities currently in use throughout Europe and in many instances the choice of modality is resource-dependent. Mindful of this, the following are guidelines as to the method and frequency of image verification.

Orthogonal Planar MV Imaging: 109 respondents in our survey use MV EPIs or MV portal films in head and neck verification.

4.5 When using MV planar imaging, orthogonal images should be acquired to verify the isocentre position. The aperture must be sufficiently large to capture relevant match structures. Image quality using orthogonal planar MV imaging is sufficient for head and neck matching. Images should be acquired with the lowest energy possible for improved contrast. The monitor units used for image acquisition should be kept as low as possible (2-5 monitor units), but should ensure adequate image quality for the matching procedure.

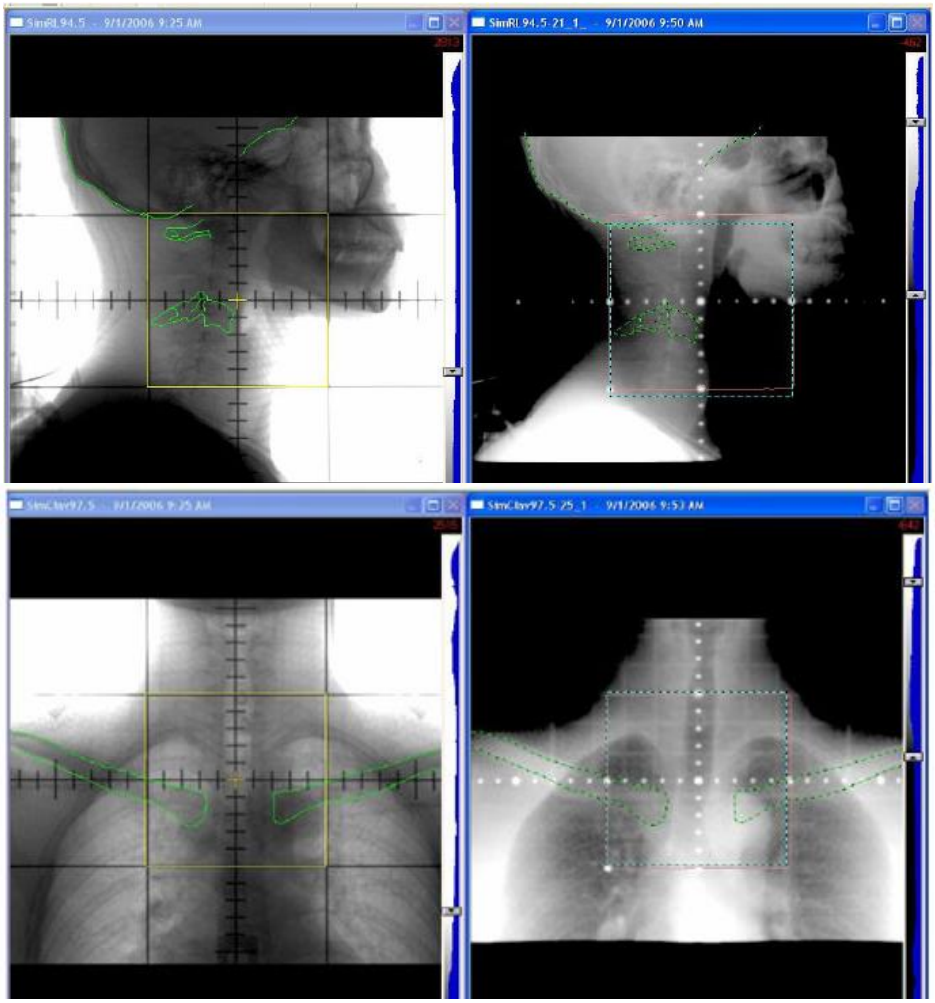

Figure 28. Orthogonal Planar MV Imaging

Orthogonal kV Imaging (On-board Imaging: OBI)

4.6 Orthogonal kV OBI has the added advantage of a large field of view and improved contrast, compared to orthogonal planar MV imaging.

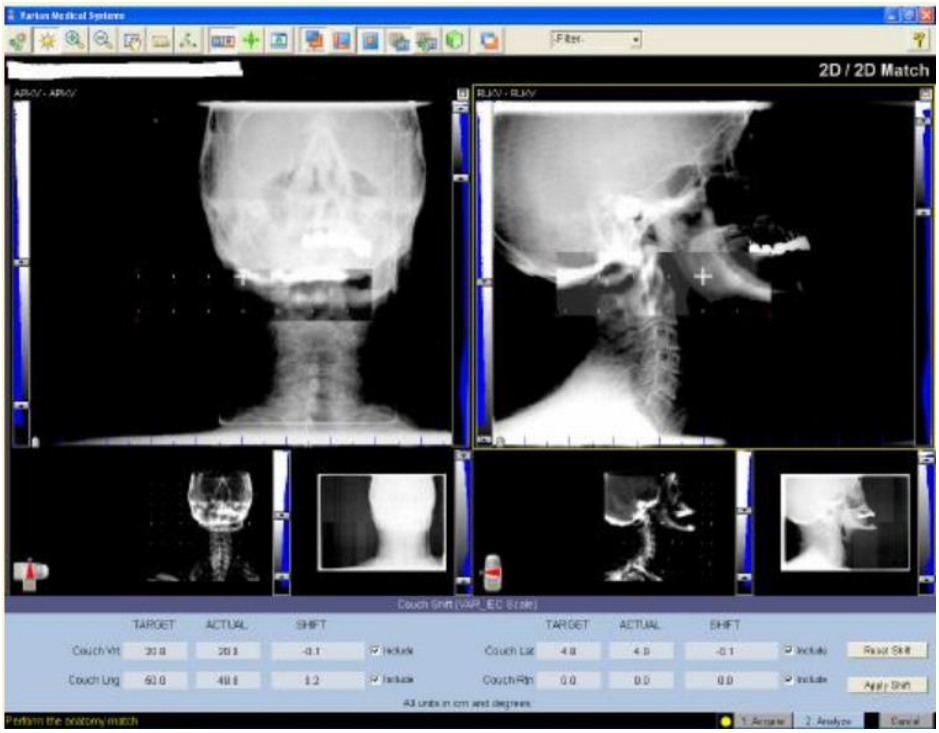

Figure 29. Orthogonal kV Imaging (OBI)

kV Cone Beam CT (CBCT)

4.7 Dose presets should be always as low reasonably achievable to obtain sufficient information on volumes and external contour, being mindful that image quality can be degraded due to scatter, noise, artefact or patient size.

4.8 3D imaging capacity brings with it additional information for the RTT about tumour and nodal shrinkage, oedema and the potential impact of weight loss on target and OAR location.

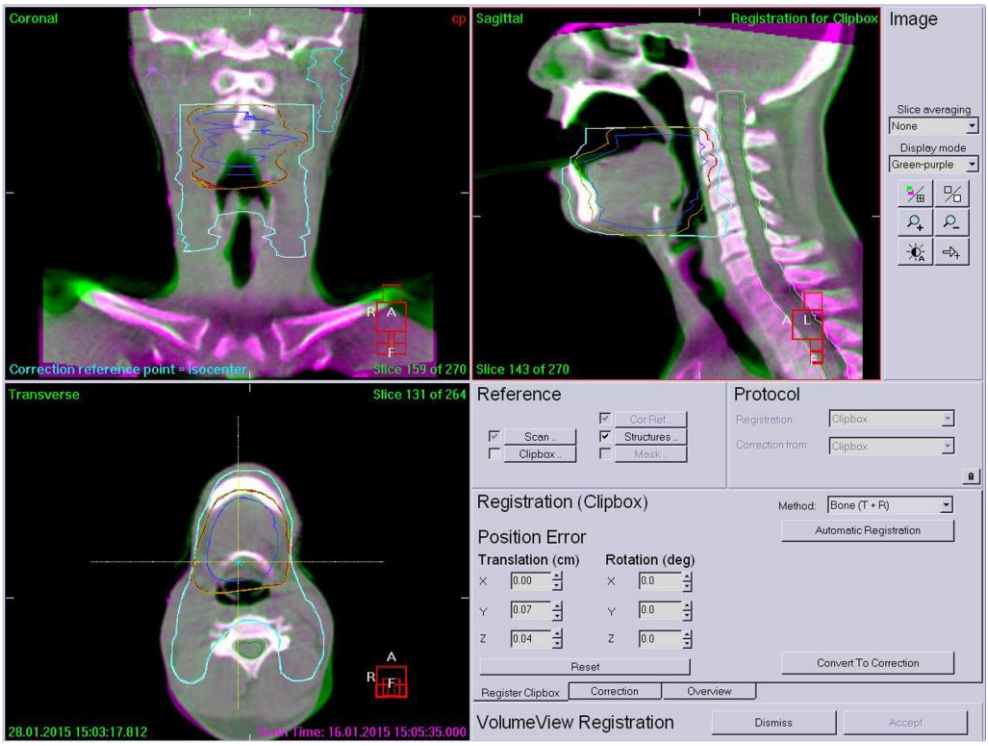

Figure 30. kV CBCT imaging

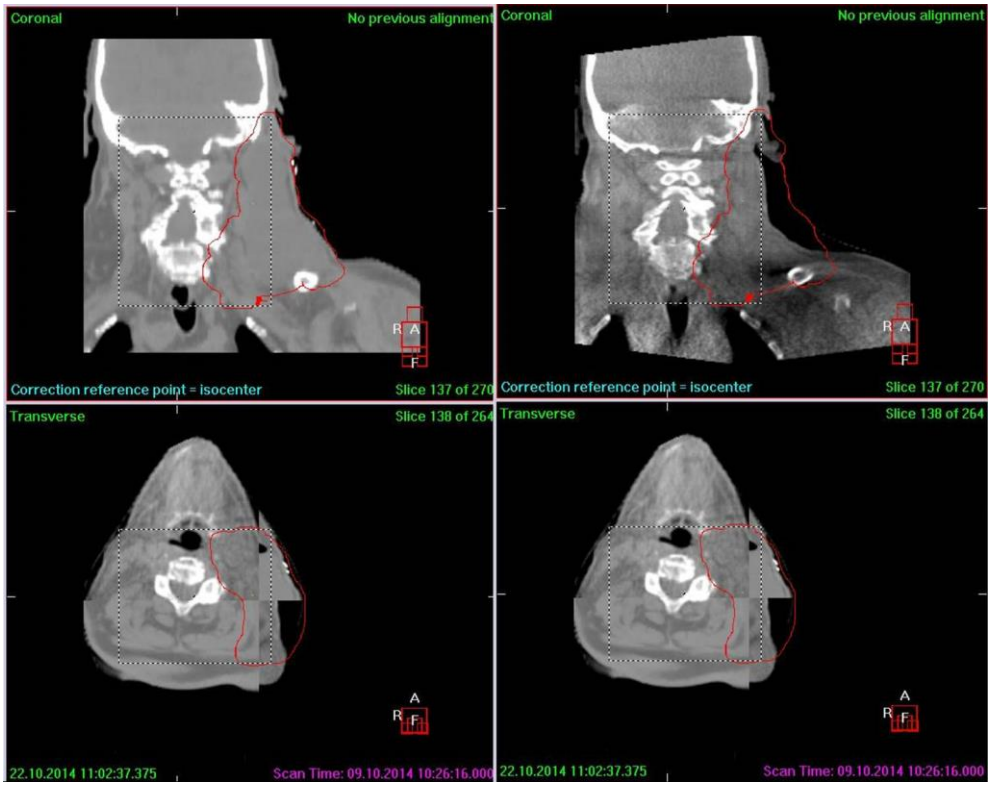

Figure 31. Tumour shrinkage as observed using kV CBCT

MVCT (MegaVoltage Computed Tomography)

4.9 The selected couch speed and imaged volume should always be as low reasonably achievable to obtain sufficient information on volumes and external contour, being mindful that image quality can be degraded due to scatter, noise, artefact or patient size.

4.10 Although kVCT systems outperform MVCT in terms of low contrast visibility, MVCT images do allow for the visualisation of tumour and nodal shrinkage, oedema and the potential impact of weight loss on target and OAR location

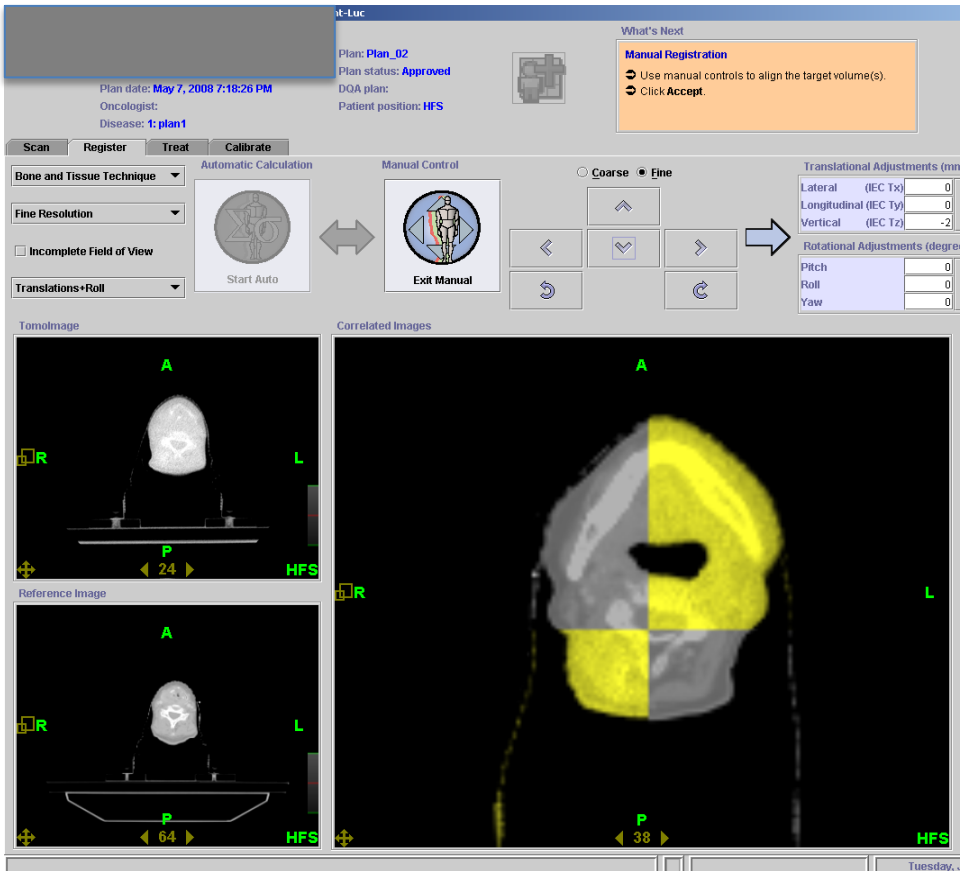

Figure 32. MVCT imaging and co-registration

Match Structures for Image Verification

4.11 Bony match structures/regions of interest (ROIs) for image verification should be a surrogate for the target and, depending on the tumour location, may include nasal septum, vertebral bodies and processes, maxilla, angle of mandible, base of skull, head of clavicle.

4.12 It may be prudent to define *primary* and *secondary* match structures at planning for use during image verification. *Primary* match structures are those whose anatomy are in close proximity to the target and are therefore most useful for position comparison and, for 3D volumetric

imaging using CBCT, will determine the position of the clipbox. *Secondary* match structures are structures whose presence is useful for guidance purposes only.

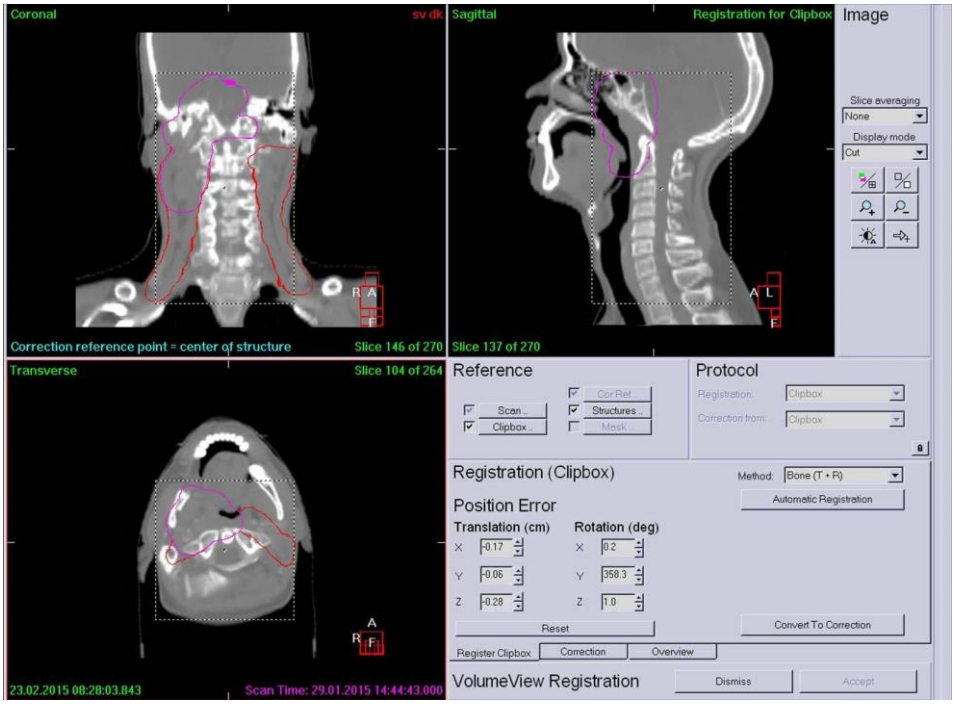

Figure 33. Clipbox Placement

Correction Protocols

Selection of online or offline correction protocol for the verification of head and neck radiotherapy patients is multifactorial and department dependent. Resources, equipment, education of staff and required patient throughput are all factors, which will be considered by individual departments when preparing such a protocol. However, it is strongly recommended that some basic principles be adhered to, irrespective of this.

4.13 Of primary concern is the reduction of the systematic error. Systematic errors are those that are generally introduced in the treatment preparation stage and hence their non-correction will result in a shift of the cumulative dose distribution. This would likely compromise both tumour control probability and normal tissue complication probability.

4.14 Offline correction strategies, such as the no-action level (NAL), extended no-action level (e-NAL) and shrinking action level (SAL) are all proven strategies to reduce the systematic error (70,71). Sourcing and correcting for the systematic error early in the course of treatment is to be recommended.

4.15 The essence of all offline correction strategies is the imaging of the patient on sequential fractions (e.g. n=3) to quantify the correction that should be applied to subsequent fractions. Images should be acquired on sequential fractions to ascertain if the error is systematic or random.

4.16 Random errors are those that generally arise in the treatment delivery phase. They are day-to-day discrepancies and result in a blurring of the cumulative dose distribution. Random errors can only be minimised using online correction strategies, that is, daily image guidance.

4.17 It is advisable that individual departments quantify their own population-based errors in order to reliably inform their choice of CTV-PTV margins for subsets of head and neck patients and to ensure that their margins are sufficient. The mechanism for this has previously been clearly outlined by others (72,73) and it is recommended that this be adhered to.

References

1. Argiris A, Karamouzis MV, Raben D and Ferris RL: Head and Neck Cancer. Lancet. 2008, 371:1695-1709.
2. Basch E, Artz D, Dulko D, Scher K, Sabbatini P, Hensley M et al: Patient online self-reporting of toxicity symptoms during chemotherapy. Journal of Clinical Oncology. 2005, 23 (15): 3552-3561
3. Burlage F, Roesink J, Kampinga H, Coppes R, Terhaard C, Langendijk J et al. Protection of salivary function by concomitant pilocarpine during radiotherapy: A double-blind, randomised, placebo-controlled study. Int. J. Radiation Oncology Biol. Phys. 2008, 70 (1): 14-22.
4. Dirix P, Abbeel S, Vansraelen B, Hermans R and Nuyts S. Dysphagia after chemoradiotherapy for head and neck squamous cell carcinoma: dose-effect relationships for the swallowing structures. Int J Radiation Oncology Biol. Phys. 2009, 75 (2): 385-392.
5. Horiot JC, Lipinski F, Schraub S, Maulard-Durdux C, Bensadoun RJ, Ardiet JM et al. Post-radiation severe xerostomia relieved by pilocarpine: A prospective French ooperative study. Radiotherapy and Oncology. 2000, 55: 233-239.
6. Jensen K. Measuring side effects after radiotherapy for pharynx cancer. Acta Oncologica. 2007, 46: 1051-1063.
7. Bentzen S, Constine L, Deasy J, Eisbruch A, Jackson A, Marks L et al. Qualitative Analyses of Normal Tissue Effect in the Clinic (QUANTEC): An introduction to the scientific issues. Int. J. Radiation Oncology Biol. Phys. 2010. 76 (Suppl 3): 3-9.
8. Henson BS, Inglehart MR, Eisbruch A, Bhide SA, Gulliford S, Kazi R et al. Preserved salivary output and xerostomia-related quality of life in head and neck cancer patients receiving parotid-sparing radiotherapy. Oral Oncolgy. 2001. 37 (1): 84-93.
9. Bhide SA, Gulliford S, Kazi R, El-Hariry I, Newbold K, Harrington KJ et al. Correlation between dose to the pharyngeal constrictors and patient quality of life and late dysphagia following chemo-IMRT for head and neck cancer. Radiotherapy and Oncology. 2009. 93: 539-544.
10. Hey J, Setz J, Gerlach R, Janich M, Sehlleier S, Schaller HG et al. Parotid-gland-sparing 3D conformal radiotherapy in patients with bilateral radiotherapy of the head and neck region-Results in clinical practice. Oral Oncology. 2009. 45: 11-17.
11. Visvanathan V and Nix P. Managing the patient presenting with xerostomia: a review. International Journal of Clinical Practice. 2010. 64 (3): 404-407.
12. Keefe DM, Schubert MM, Elting LS, Sonis ST, Epstein JB, Raber-Durlacher JE et al. Update clinical practice guidelines for the prevention and treatment of mucositis. Cancer. 2007. 109: 820-831.
13. Logemann, J: Mechanism of normal and abnormal swallowing. In: Otolaryngology: Head and Neck Surgery. 5th edition. Edited by Cummings, JW, Flint PW, Haughey BA et al. St Louis: Mosby; 2008.
14. Levendag P, Teguh D, Voet P et al. Dysphagia disorders in patients with cancer of the oropharynx are significantly affected by the radiation therapy dose to the superior and middle constrictor muscle: a dose-effect relationship. Radiotherapy and Oncology. 2007: 85 (1): 64-73.
15. Leslie P, Carding PN, Wilson JA. Investigation and management of chronic dysphagia. British Medical Journal. 2003. 326: 433-436.
16. Roe JW, Carding PN, Dwivedi RC, Kazi RA, Rhys-Evans PH, Harrington KJ et al. Swallowing outcomes following Intensity Modulated Radiation Therapy (IMRT) for head and neck cancer- a systematic review. Oral Oncology. 2010. 46 (10): 727-733.
17. Kulbersh BD, Rosentahl EL, McGRew BM et al. Pretreatment, preoperative swallowing exercises may improve dysphagia quality of life. Laryngoscope. 2006. 116: 883-886.
18. Logemann JA. The role of exercise programmes for dysphagia patients. Dysphagia. 2005. 20: 139-140.
19. Caglar HB, Tishler RB, Othus M, Burke E, Li Y, Goguen L et al. Dose to larynx predicts for swallowing complications after intensity-modulated radiotherapy. Int. J. Radiation Oncology Biol. Phys. 2008, 72 (4): 1110-1118.

20. Hovan AJ, Williams M, Stevenson-Moore P, Wahlin YB, Ohrn KEO, Elting L, Spijkervet FKL et al. A systematic review of dysgeusia induced by cancer therapies. Supportive Care Cancer. 2010. 18: 1081-1087.

21. Hong JH et al. Taste and odour abnormalities in cancer patients. Journal Supportive Oncology. 2009. 7(2): 58-65.

22. Ripamonti C. Taste alterations in cancer patients. Journal Pain Symptom Management. 1998. 16 (6): 349-351.

23. Halyard MY, Jatoi A, Sloan JA, Bearden JD 3rd, Vora SA, Atherton PJ et al. Does zinc sulphate precent therapy-induced taste alterations in head and neck cancer patients? Results of phase III double-blind, placebo-controlled trial from the North Central Cancer Treatment Group (N01C4) Int. J. Radiation Oncology Biol. Phys. 2007. 67 (5): 1318-1322.

24. Ravasco P et al. Impact of nutrition on outcome: a prospective randomized controlled trial in patients with head and neck cancer undergoing radiotherapy. Head and Neck. 2005. 27: 659-668.

25. Dijkstra PU, Kalk WW and Roodenburg JL. Trismus in head and neck oncology: a systematic review. Oral Oncolgoy. 2004. 40: 879-889.

26. Bensadoun RJ, Risenbeck D, Lockhart P< Elting L, Spijkervert F and Brennan M. A systematic review of trismus induced by cancer therapies in head and neck cancer patients. Supportive Care Cancer. 2010. 18: 1033-1038.

27. Bentel GC, Marks LB, Hendren K, Brizel DM. *Comparison of two head and neck immobilization systems.* Int J Radiation Oncol Biol Phys. 1997. 1:38 (4): 867-873.

28. Hong TS, Tome WA, Chappell RJ, Chinnaiyan P, Mehta MP, Harari PM. The impact of daily setup variations on head and neck intensity modulated radiaiton therapy. Int J Radiation Oncol Biol Phys. 2005. 61(3):779-88.

29. Sharp L, Lewin F, Johansson H, Payne D, Gerhardsson A, Rutqvist LE. Randomised trial on two types of thermoplastic masks for patient immobilisation during radiation therapy for head and neck cancer. Int J Radiation Oncol Biol Phys. 2005. 61(1):250-6.

30. Karger CP, Jäkel O, Debus J, Kuhn S, Hartmann GH. Three-dimensional acuracy and interfractional reproducibility of patient fixation and positioning using a stereotactic head mask system. Int J Radiation Oncol Biol Phys. 2001. 49 (5): 1493-1504.

31. Willner J, Hädinger U, Neumann M, Schwab FJ, Bratengeier K, Flentje M. *Three dimensional variability in patient positioning using bite block immobilization in 3D-conformal radiation treatment for ENT-tumors.* Radiother Oncol. 1997. 43(3):315-21.

32. McKernan B, Bydder SA, Deans T, Nixon MA, Joseph DJ. *Surface laser scanning to routinely produce casts for patient immobilization during radiotherapy.* Australas Radiol. 2007. 51(2):150-3.

33. Boda-Heggemann J, Walter C, Rahn A, Wertz H, Loeb I, Lohr F and Wenz F. Int J Radiat Oncol Biol Phys. 2006. 1;66 (5): 1568-1575.

34. Donato K, Leszczynski K and Fleming K. A comparative evaluation of two head and neck immobilisation devices used during electronic portal imaging. Br J Radiol. 2006. 79 (938): 158-161.

35. Humphreys M, Guerrero Urbano MT, Mubata C, Miles E, Harrington KJ, Bidmead M et al. Assessment of a customised immobilisation system for head and neck IMRT using electronic portal imaging. Radiother. Oncol. 2005. 77(1): 39-44.

36. Kang H, Lovelock DM, Yorke ED, Kriminski S, Lee N and Amols HI. Accurate positioning for head and neck cancer patients using 2D and 3D image guidance. J Appl Clin Med Phys. 2010. 12 (1): 3270.

37. Kassaee A, Das IJ, Tochner Z, et al. Modification of Gill-Thomas-Cosman frame for extracranial head-and-neck stereotactic radiotherapy. Int J Radiation Oncol Biol Phys 2003. 57(4): 1192-1195.

38. Velec M, Waldron JN, O'Sullivan B, Bayley A, Cummings B, Kim JJ et al. Cone-beam CT assessment of interfraction and intrafraction setup error of two head and neck cancer thermoplastic masks. Int J Radiation Oncol Biol Phys. 2010. 76 (3): 949-955.

39. Ahn PH, Ahn AI, Lee CJ, Shen J, Miller E, Lukaj A et al. Random positional variation among the skull, mandible and cervical spine with treatment progression during head and neck radiotherapy. INt J Radiation Oncol Biol Phys. 2009. 73 (2): 626-633.

40. Bale RJ, Sweeney R, Vogele M, Nevinny M, Auer T, Bluhm A et al. Noninvasive head fixation for external irradiation of tumours of the head and neck area. Strahlenther Onkol. 1998. 174 (7): 350-354.

41. Fairclough-Tompa L, Laresen T and Jaywant SM. Immobilisation in stereotactic radiotherapy: the head and neck localiser frame. Medical Dosimetry. 2001. 26(3): 267-273.

42. Gilbeau L, Octave-Prignot M, Loncol T, Renard L, Scalliet P and Gregoire V. Comparison of setup accuracy of three different thermoplastic masks for the treatment of brain and head and neck tumours. Radiother Oncol. 2001. 58 (2): 155-162.

43. Rotondo RL, Sulltanem K, Lavoie I, Skelly J and Rymond L. Comparison of repositioning accuracy of two commercially available immobilisation systems for treatment of head and neck tumours using simulation computed tomography imaging. Int J Radiation Oncol Biol Phys. 2008. 70 (5): 1389-1396.

44. Neubauer E, Dong L, Followill DS, Garden AS, Court LE, Allen White R et al. Assessment of shoulder position variation and its impact on IMRT and VMAT doses for head and neck cancer. Radiation Oncology. 2012. 7:19 doi: 10.1186/1748-717X-7-19.

45. Linthout N, Verellen D, Tournel K and Storme G. Six-dimensional analysis with daily stereoscopic x-ray imaging of intrafraction patient motion in head and neck treatments using five point fixation masks. Med Phys. 2006. 33 (2): 504-513.

46. Bentel GC, Marks LB, Sherouse GW and Spencer DP. A customised head and neck support system. Int J. Radiation Oncol Biol Phys. 1995. 32 (1): 245-248.

47. Marsh R, Balter J, Evans VL and Eisbruch A. Design and analysis of an immobilisation and repositioning system for treatment of neck malignancies. Medical Dosimetry. 1997. 22 (4): 293-297.

48. Li H, Zhu XR, Zhang L, Dong L, Tung S, Ahamad A et al. Comparison of 2D radiographic images and 3D cone beam computed tomography for positioning head-and-neck radiotherapy patients. Int J Radiation Oncol Biol Phys. 2008. 71 (3): 916-925.

49. Houweling AC, van der Meer S, van der Wal E, Terhaard CH and Raaijmakers CP. Improved immobilisation using an individual head support in head and neck cancer patients. Radiother Oncol. 2010. 96 (1): 100-103.

50. Prisciandaro JI, Frechette CM, Herman MG, Brown PD, Garces YI and Foote RL. A methodology to detremine margins by EPID measurements of patient setup variation and motion as applied to immboilisation devices. Med. Phys. 2004. 31 (11): 2978-2988.

51. Van Lin EN, van der Vight L, Huizenga H, Kaanders JH and Visser AG. Set-up improvement in head and neck radiotherapy using a 3D off-line EPID-based correction protocol and a customised head and neck support. Radiother. Oncol. 2003. 68 (2): 137-148.

52. Fiorino C, Cattaneo GM, Del Vecchio A, Fusca M, Longobardi B, Signorro P et al. Skin-sparing reduction effects of thermoplastics used for patient immobilisation in head and neck radiotherapy. Radiother. Oncol. 1994. 30 (3): 267-270.

53. Ezzell LC, Hansen EK, Quivey JM and Xia P. Detection of treatment setup errors between two CT scans for patients with head and neck cancer. Med Phys. 2007. 34 (8): 3233-3242.

54. Kang H, Lovelock DM, Yorke ED, Kriminski S, Lee N and Amols HI. Accurate positioning for head and neck cancer patients using 2D and 3D image guidance. J Appl Clin Med Phys. 2010. 12 (1): 3270.

55. Sijtsema NM, van den Burgh AC, Burlage FR, Bijl HP, Langendijk JA and Meertens H. Patient position verification with oblique radiation beams. Radiother Oncol. 2007. 85 (1): 126-131.

56. Ove R, Cavalieri R, Noble D and Russo SM. Variation of neck position with Image-guided radiotherapy for head and neck cancer. Am J Clin Oncol. 2012. 35 (1): 1-5.

57. Giske K, Stoiber EM, Schwarz M, Stoll A, Muenter MW, Timke C et al. Local setup errors in image-guided radiotherapy for head and neck cancer patients immobilised with a custom-made device. Int J Radiation Oncol Biol Phys. 2011. 80 (2): 582-589.

58. Oita M, Ohmori K, Obinata K, Kinoshita R, Onimaru R, Tsuchiya K et al. Uncertainty in treatment of head and neck tumours by use of intraoral mouthpiece and embedded fiducials. Int. J. Radiation Oncol Biol Phys. 2006. 64 (5): 1581-1588.

59. McKernan B, Bydder S, Ebert M, Waterhouse D and Joseph D. A simple and inexpensive method to routinely produce customised neck supports for patient immobilisation during radiotherapy. J Med Imaging Radiat Oncol. 2008. 52 (6): 611-616.

60. Schubert LK, Westerly DC, Tomé WA, Mehta MP, Soisson ET, Mackie TR et al. A comprehensive assessment by tumor site of patient setup using daily MVCT imaging from more than 3,800 helical tomotherapy treatments. Int J Radiation Oncol Biol Phys. 2009. 73(4):1260-9.

61. Johansen J, Bertelsen A, Hansen CR, Westberg J, Hansen O and Brink C. Set-up errors in patients undergoing image guided radiation treatment. Relationship to body mass index and weight loss. Acta Oncol. 2008. 47(7): 1454-1458.

62. Pehlivan B, Pichenot C, Castaing M, et al. Interfractional set-up errors evaluation by daily electronic portal imaging of IMRT in head and neck cancer patients. Acta Oncol 2009. 48(3) :440-5.

63. Gupta T, Chopra S, Kadam A, et al. Assessment of three-dimensional set-up errors in conventional head and neck radiotherapy using electronic portal imaging device. Radiation Oncology. 2007. 2(44):44.

64. Vaandering A, Lee JA, Renard L and Gregoire V. Evaluation of MVCT protocols for brain and head and enck tumour patients treated with helical tomotherapy. Radiother Oncol. 2009. 93 (1): 50-56.

65. Bertelsen A, Nielsen M, Westberg J, Jensen HR, Brink C. The representitativeness of patient position during the first treatment fractions. Acta Oncol. 2009. 48(2):259-66.

66. Siebers JV, Keall PJ, Wu Q, Williamson JF and Schmidt-Ullrich RK. Effect of patient set-up errors on simultaneously integrated boost head and neck IMRT treatment plans. Int. J. Radiation Oncol Biol Phys. 2005. 63 (2): 422-433.

67. Yu Y, Michaud AL, Sreeraman R, Liu T, Purdy JA and Chen AM. Comparison of daily versus non-daily image-guided radiotherapy protocols for patients treated by intensity-modulated radiotherapy for head and neck cancer. Head Neck. 2013.

68. Kapanen M, Laaksomaa M, Tulijok T, Peltola S, Wigren T, Hyodynmaa S et al. Estimation of adequate setup margins and threshold for position errors requiring immediate attention in head and neck cancer radiotherapy based on 2D image guidance. Radiation Oncology. 2013, 8:212. doi:10.1186/1748-717X-8-212

69. Simpson DR, Lawson JD, Nath SK, Rose BS, Mundt AJ and Mell LK. A survey of Image-guided Radiation Therapy Use in the United States. Cancer. 2010. 15:116(16): 3953-3960.

70. De Boer HC and Heijmen B. A protocol for the reduction of systematic patient setup errors with minimal portal imaging workload. Int J Radiat Oncol Biol Phys. 2001. 50(5): 1350-1365.

71. De Boer HC and Heijmen B. eNAL: an extension of the NAL setup correction protocol for effective use of weekly follow-up measurements. Int J Radiat Oncol Biol Phys. 2007. 67(5): 1586-1595.

72. The Royal College of Radiologists, Society and College of Radiographers, Institute of Physics in Engineering and Medicine. On target: ensuring geometric accuracy in radiotherapy. London: The Royal College of Radiologists, 2008.

73. Van Herk M. Errors and margins in radiotherapy. Seminars in Radiation Oncology. 2004.14(4): 322-325.

Bibliography

Mencarelli A, van Beek S, van Kranen S, Rasch C, van Herk M, Sonke JJ. Validation of deformable registration in head and neck cancer using analysis of variance. *Med Phys* 2012 November;39(11):6879-84.

van Beek S, van Kranen S, Mencarelli A et al. First clinical experience with a multiple region of interest registration and correction method in radiotherapy of head-and-neck cancer patients. *Radiother Oncol* 2010 February;94(2):213-7.

van Kranen S, van Beek S, Rasch C, van Herk M, Sonke JJ. Setup uncertainties of anatomical sub-regions in head-and-neck cancer patients after offline CBCT guidance. *Int J Radiat Oncol Biol Phys* 2009 April 1;73(5):1566-73.