



Randomised clinical trial testing a 1-week course of curative whole breast radiotherapy against a standard 3-week schedule in terms of local cancer control and late adverse effects in patients with early breast cancer

Guidelines to outlining, planning and delivery of lymphatic radiotherapy for FAST-Forward trial patients

**Lymphatic RT QA Pack
v. 1.1 July 2016**

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Details of amendments to the Guidelines to outlining, planning and delivery of lymphatic radiotherapy for FAST-Forward trial patients

Guidelines Version 1.1

- Table 1: Additional sentence included for outlining of level 1-, 'The craniolateral border of level 1 should be delineated up to a 1cm inf and medial to the humeral head. Creation of a 1cm humeral head PRV may be used to guide delineation.'
- Section 2.2: Specification of prescription point reworded.
- Section 2.5: Constraints categorised.
- Section 4.0: Only the first patient randomised will be prospectively reviewed.

Foreword

This document contains guidelines to outlining, planning and delivery of lymphatic radiotherapy for FAST-Forward trial patients as described in FAST-Forward protocol version 3.0 8th July 2015. This document does not replace the main trial FAST-Forward planning pack (v.3.0 May 2013), which details the treatment to the whole breast or chest wall, and is to be used in conjunction with it.

This document should not be used as a guide for the treatment of patients outside of the FAST-Forward trial. All outlining, treatment planning and delivery queries should be directed to the contacts on the next page.

Every care has been taken in drafting these guidelines but corrections or amendments may be necessary. These will be circulated to Investigators and treatment planning and physics staff, but centres are advised to contact the FAST-Forward RTTQA lead to confirm they have the most recent and approved version.

Contacts

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1 Scanning and outlining

It is a prerequisite of the FAST-Forward trial that the lymph node clinical and planning target volumes (CTV and PTV) be delineated. These should be outlined in addition to all target structures required for the whole breast or chest wall radiotherapy, details for which are given in the main trial planning pack currently in place.

It is strongly recommended that the combined lymph node PTV is encompassed within a traditional nodal field as previous studies have shown that recurrences occur within field. Therefore, larger volumes are unnecessary and could cause increased toxicity.

The CT scan used for planning for nodal patients should extend from mid-neck to below the diaphragm. Intravenous contrast may be used to facilitate the outlining process, but is not a requirement for the trial.

1.1 Target Volumes

It is essential to ensure that all structure names comply with the trial protocol and planning guidelines nomenclature, to ensure consistency amongst all patients recruited to FAST-Forward and facilitate data analysis.

1.1.1 Lymph node Clinical Target Volume

The lymph node clinical target volume (**LN CTV**) may include the supraclavicular nodes (defined as level 4 in accordance with the ESTRO nodal outlining consensus guidelines [1]) and/or the axillary chain. The axillary chain can be treated in its entirety or only the levels specified by the clinician. As the lymph nodes themselves are not easily visualised on CT (unless they are enlarged) anatomical landmarks clearly identifiable on the images can be used to outline the LN CTV, as detailed in Tables 1 below. All nodal groups are illustrated on the two example cases in Appendix 1.

Please note that Table 1 and the example cases in Appendix 1 provide details on the individual nodal levels and should be used as a guide to where they would be located. For the trial all nodal levels to be treated should be outlined in continuity as one nodal CTV volume.

Table 1: CT landmarks for the breast nodal groups (Adapted from Offeren et al, 2015 [1])

CT scan margin	Nodal group				
	Level 4	Level 3	Interpectoral nodes	Level 2	Level 1 (including visible scarring)
Cranial	Includes the cranial extent of the subclavian artery (i.e. 5 mm cranial of subclavian vein)	Includes the cranial extent of the Subclavian artery (i.e. 5 mm cranial of subclavian vein)	Includes the cranial extent of the axillary artery (i.e. 5 mm cranial of axillary vein)	Includes the Cranial extent of the axillary artery (i.e. 5 mm cranial of axillary vein)	Medial: 5 mm cranial to the axillary vein Lateral: max up to 1 cm below the edge of the humeral head, 5 mm around the axillary vein
Caudal	Includes the subclavian vein with 5 mm margin, thus connecting to the cranial border of IMN.	5 mm caudal to the subclavian vein. If appropriate: top of surgical ALND	Level 2's caudal limit	The caudal border of the minor pectoral muscle. If appropriate: top of Surgical ALND	The level of rib 4 – 5, taking also in to account the visible effects of the sentinel lymph node biopsy
Ventral	Sternocleidomastoid muscle, dorsal edge of the clavicle	Major pectoral muscle	Major pectoral muscle	Minor pectoral muscle	Pectoralis major & minor muscles
Dorsal	Pleura	Up to 5 mm dorsal of Subclavian vein or to costae and Intercostal muscles	Minor pectoral muscle	Up to 5 mm dorsal of axillary vein or to costae and intercostal muscles	Cranially up to the thoraco-dorsal vessels, and more caudally up to an imaginary line between the anterior edge of the latissimus dorsi muscle and the intercostal muscles
Medial	Including the jugular vein without margin; excluding the thyroid gland and the common carotid artery	Junction of subclavian and internal Jugular veins – >level 4	Medial edge of minor pectoral muscle	Medial edge of minor Pectoral muscle	Level 2, the Interpectoral level and the thoracic wall
Lateral	Includes the anterior scalene muscles and connects to the medial border of Level 3.	Medial side of the minor Pectoral muscle	Lateral edge of minor pectoral muscle.	Lateral edge of minor pectoral muscle	Cranially up to an Imaginary line between the major pectoral and deltoid muscles, and further caudal up to a line between the major pectoral and latissimus dorsi muscles. (The craniolateral border of level 1 should be delineated up to a 1cm inf and medial to the humeral head. Creation of a 1cm humeral head PRV may be used to guide delineation.)

1.1.2 Lymph node Planning Target Volume

The **LN PTV** is created from the LN CTV by applying an appropriate expansion margin. Suggested margins are 5-10 mm; however for a level 4 region a maximum of 5 mm margin should be applied medially in order to limit the dose to midline structures. If there is concern about the dose to midline structures this margin can be further restricted (Fig. 1).

Once the superior border of the tangent fields has been identified to include the extent of the breast tissue/chestwall the relative location of the nodal CTV can be considered accordingly. Limited or no expansion may be applied inferiorly depending on the position of the superior border of the tangential fields for a CTV not inclusive of level 1.

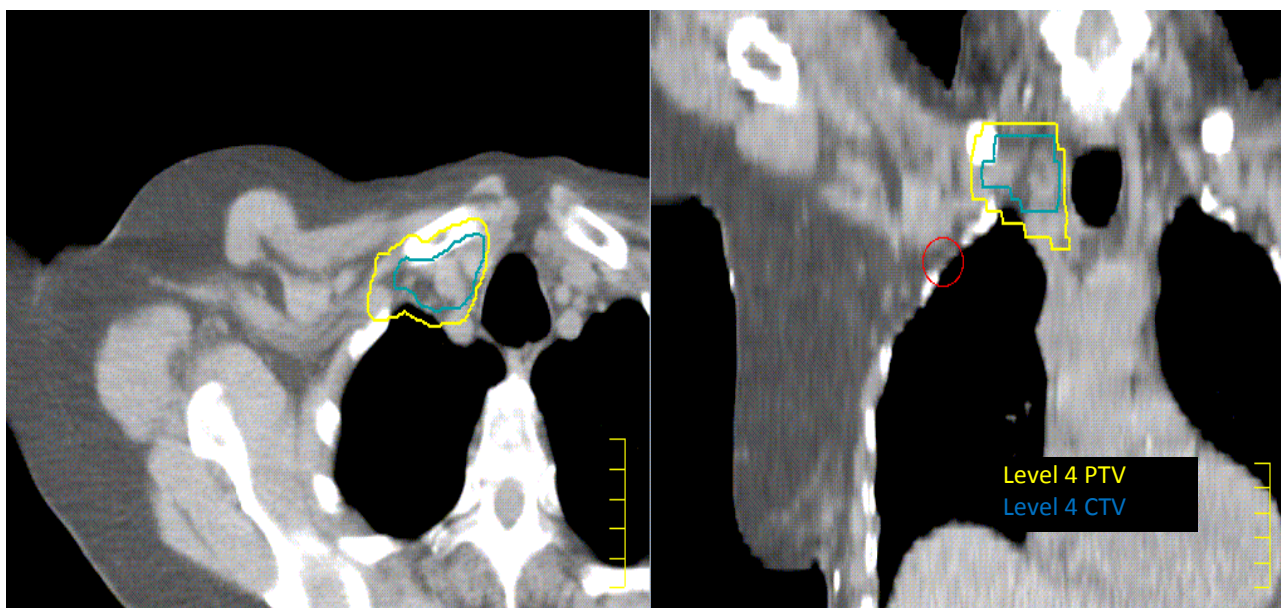


Fig. 1: Limited medial CTV-PTV margin for level 4 nodes

1.1.3 Plan evaluation volume

An additional structure **LN PTV DVH** should be created for plan evaluation purposes only, by cropping the LN PTV 5 mm from the skin, lung and field borders to avoid dose calculation in penumbra and build-up regions. All DVH objectives stated in the plan assessment form refer to the plan evaluation volume and should be reported to it rather than to the original uncropped LN PTV volume. Please note that when level 1 is outlined the caudal extent within the tangent fields will not be included.

1.2 Organs at risk

In addition to the ipsilateral lung and heart for the purposes of the trial the **Brachial Plexus** should be outlined for all patients receiving lymph node radiotherapy. The axillary bundle (nerve, artery, and vein) should be identified in the axilla and traced back to the rib cage. In this region the artery should be outlined to represent the brachial plexus, which surrounds this vessel. A 5-mm diameter paint tool can be used to contour the brachial plexus OAR [2].

The lower brachial plexus passes between the anterior and middle scalene muscles, from the exit foramina of the C7 and T1 vertebrae. This route should be outlined where present in the CT slices. The resulting volume represents the lower brachial plexus.

An example for the outlining of the brachial plexus is provided in Appendix 1.

2 Planning

2.1 Field matching technique

Centres can use either single or dual isocentre technique. The position of the isocentre should be considered carefully if posterior fields are to be used, to avoid potential collision with the couch.

Matching of the inferior border of the level 4 and axillary fields to the superior border of the whole breast or chest wall tangential fields should preferably be achieved using non-divergent field edges. For single isocentre technique this can be achieved by asymmetry. In dual isocentre techniques non-divergent field edges can be achieved by using a combination of couch and collimator rotation angles in conjunction with asymmetry, or angle combinations alone. Appropriate machine QA procedures should be in place to verify the accuracy of the asymmetric field set-up [3].

The method of field matching used at investigator sites should ensure the adequate coverage of the target while at the same time avoiding tissue overdose at the match line, and will be subject to approval by the RTTQA group.

2.2 Dose fractionation

The dose prescribed to level 4 and/or axilla should be as follows:

Control group:	40.05 Gy in 15 fractions
Test group 1:	27 Gy in 5 fractions
Test group 2:	26 Gy in 5 fractions

2.3 Prescription point

Dose should be prescribed to a clinically relevant point within the LN PTV in accordance with ICRU.

2.4 Beam parameters

The beam should be shaped to cover fully the LN PTV using MLC (with an appropriate penumbra margin), but care should be taken to avoid the oesophagus and the trachea medially (refer to 1.1.2). Please be aware that following expansion of the LN CTV a gap may be apparent between the tangential fields and the caudal border of the nodal levels 2/3/4. It is recommended that no MLC shield this region avoiding cold regions between the tangential field and nodal fields.

When treating nodal levels 2-4 a single anterior field is recommended, which can be angled as required avoiding the spinal cord (with an appropriate margin) and/or any overlap with the tangential fields.

If the level 1 axilla is to be part of the CTV it should be noted that the inferior part of level 1 overlaps with the breast tissue and will be included in the main breast/chest wall fields. The posterior border of the tangents may therefore be amended to ensure coverage at depth to both breast and axilla level 1, with potential increase in lung dose/coverage considered accordingly by the referring clinician.

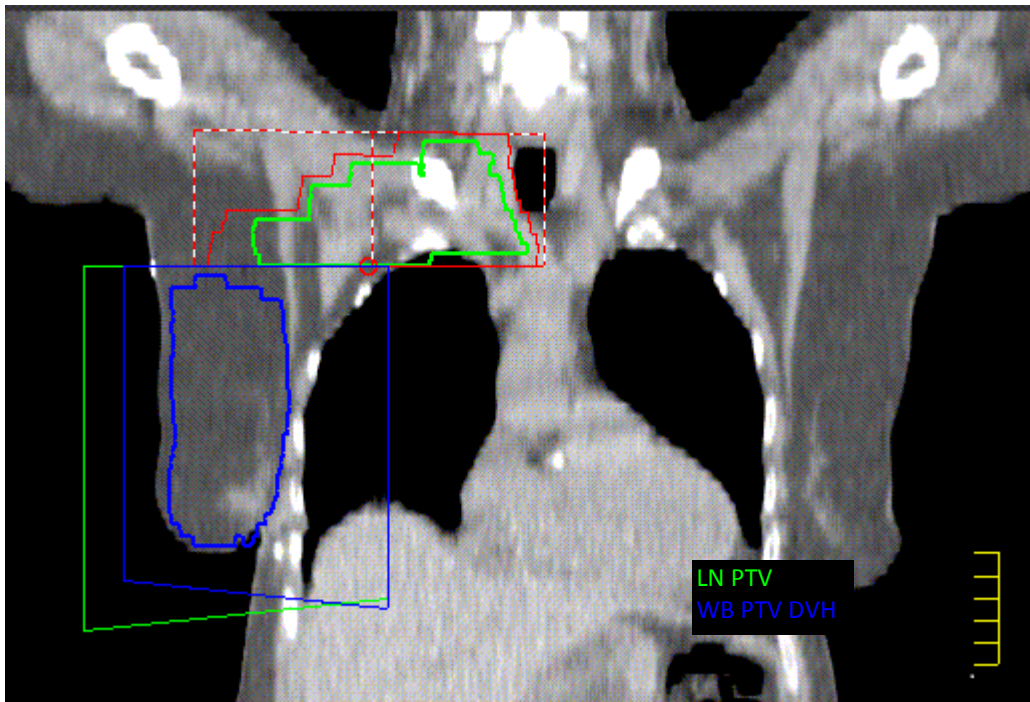


Fig. 2: Example nodal field

Appropriate beam energies should be used depending on the depth of the nodal volume, in order to optimise coverage and reduce hotspots. Where necessary, planners should consider using photon energies higher than 6 MV.

In some cases a single anterior beam might not be sufficient to provide adequate coverage to the LN PTV, and planners should consider the use of a higher energy posterior field, if this is in compliance with the local planning protocol. It is likely to be weighted down compared with anterior. The weight of the posterior field should be as low as possible to limit unnecessary exposure to the surrounding normal tissue however it should be sufficient to ensure adequate coverage to the nodal PTV volume and to decrease the dose maximum anteriorly to the tolerance specified below.

In cases where the clinical oncologist would like to give radiotherapy to axilla levels 1 and 2 only, depending on the patient's anatomy it might be possible to achieve the required coverage to the LN PTV using high tangents only, without using additional nodal field(s). This is likely to be the exception. This is acceptable if all target and OAR constraints are met, but should be discussed with the trial QA team in advance. Please note that this option can be considered for treatment of nodal levels 1 and 2 only, and is not allowed if radiotherapy is given to levels 3 and 4 as well.

It is expected that a simple anterior field for treating levels 3 and 4 only and the addition of a posterior field arrangement for treating a CTV inclusive of level 1 will be sufficient in meeting the dose constraints. Please contact the QA team if planning takes longer than 1.5 times the amount of time spent on routine breast patients with nodal treatment.

The use of rotational techniques to treat the breast/chest wall and nodal regions is not recommended in the FAST-Forward trial. Please contact the QA team in advance if these are being considered.

Deep inspiration breath hold can be used when treating FAST-Forward patients, and this should be noted on the plan assessment form.

2.5 Plan evaluation

The coverage and hotspots to both breast and nodal target regions must be assessed in the treatment planning system using the **composite** of the two dose distributions, including all breast and nodal fields.

In addition to the DVH constraints specified in the main trial FAST-Forward planning pack (v. 3 May 2013), planners should aim to achieve the following dose distribution objectives.

Optimal Objectives:

- LN PTV DVH coverage $V_{90\%} \geq 90\%$
- $V_{107\%} \leq 2\%$ of LN PTV DVH.
- $V_{107\%} \leq 2 \text{ cm}^3$ outside the nodal and breast/chest wall PTV volumes
- Maximum point dose should not exceed 110% of the prescribed dose.
- The maximum dose to 0.1 cm^3 the brachial plexus should not exceed 105% of the prescribed dose.
- Ipsilateral Lung $V_{30\%} \leq 25\%$

Dose to the organs at risk from the composite plan should be kept as low as possible. The lung and heart normal tissue constraints given in the main trial FAST-Forward planning pack (v. 3 May 2013) should be used to assess the **whole breast or chest wall plan only** without any nodal field dose contribution. A Plan Assessment Form (PAF) should be completed for each patient. Please make sure all cells are completed correctly. **All forms should be submitted in electronic format.**

In selected circumstances deviations from the tolerances stated above may be required. These should be at the discretion of the clinical oncologist in charge, should be reported and justified, and the QA team should be contacted before the patient starts treatment.

3 Verification

For control group patients treatment verification is required for at least the first three fractions and then weekly. It is best practice to correct all systematic errors after the first three fractions however if a centre wishes to use a correction tolerance on systematic error it should not be greater than 5 mm, and preferably not more than 3 mm. The correction is carried out following local practice as long as this has been approved by the QA team.

Any correction is applied on fraction 4, with imaging to confirm the move. A suitable tolerance for the check of the correction is 5 mm. Verification is then done once weekly throughout the remaining treatment with a tolerance of 5 mm.

Verification imaging is required on each fraction for test group patients, in order to check for gross error prior to treatment. A tolerance of not more than 5 mm should be used. Local policy is followed if the check is out of tolerance.

For single isocentre technique the verification should be carried out for the whole breast/chest wall and nodal fields together before treating the main tangents. For double isocentre technique the tangents should be verified and treated first. Once the tangents have been treated, only lateral adjustments can be made on the nodal field and the match line should not be changed.

For all treatment groups when applying corrections in set-up all necessary precautions should be taken to avoid overlap/underdosage at the match between the nodal field and the main tangents.

4 Quality assurance

All centres are required to successfully complete the lymphatic RT QA programme in addition to that previously undertaken as part of FAST-Forward.

The FAST-Forward Nodal study QA programme consists of:

- Lymphatic Outlining Benchmark case- **Please note each clinician recruiting patients to FAST-Forward will be required to have obtained outlining QA approval.**
- Lymphatic Planning Benchmark case- QA of the planning technique will be performed at each participating centre by planning the pre-outlined test patient
- Process Document- Submission of an amended process document detailing additional information in relation to treatment of patients randomised to the nodal study.
- Prospective review
 - Prospective review of the nodal CTV and radiotherapy plan will be performed for the first patient recruited from each centre prior to the patient starting treatment.

The QA group will review and report back to the investigator site within 48 hours of receipt of data (provided sufficient notice is given) for prospective reviews. If any major protocol deviations are identified, additional reviews may be requested.

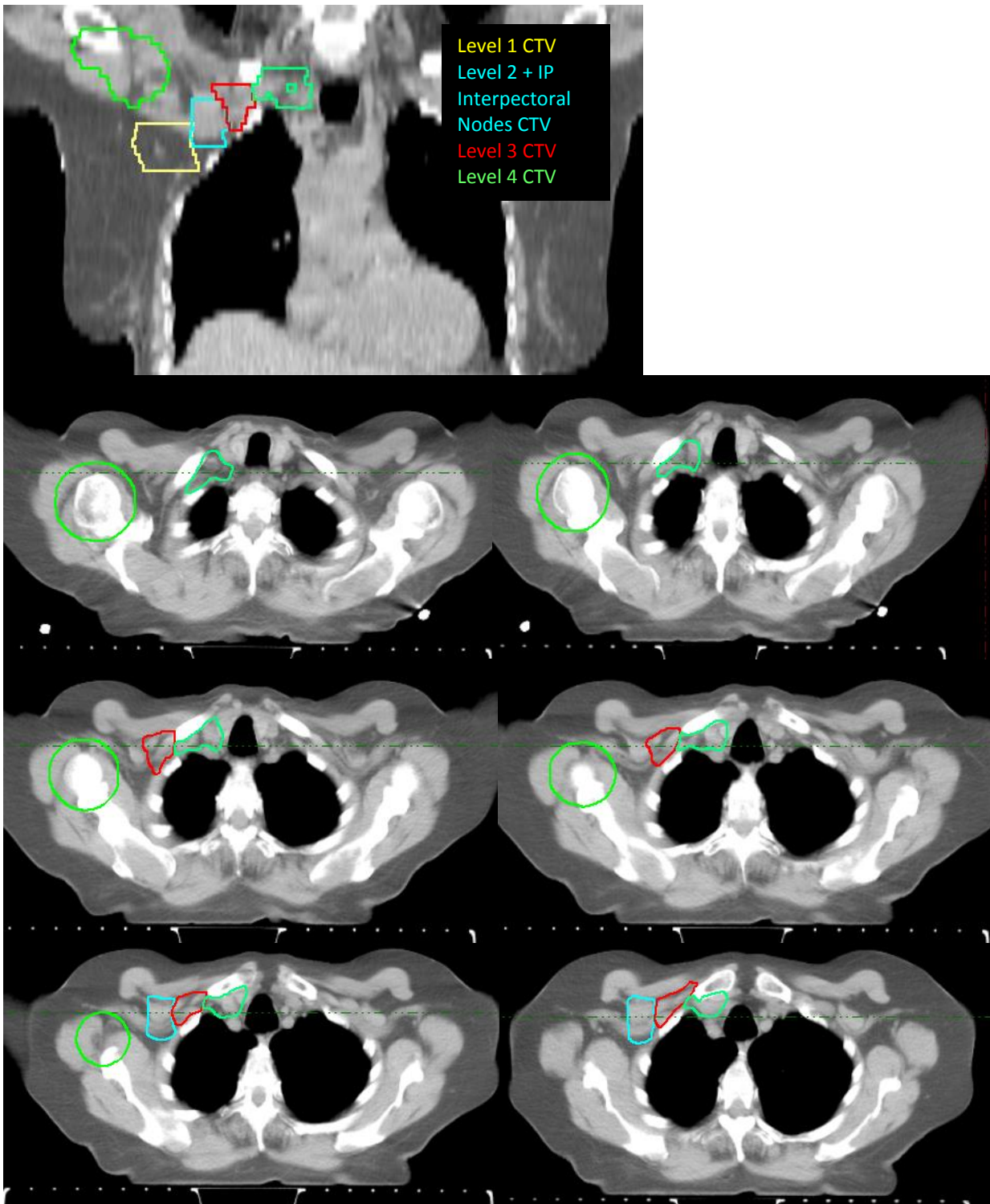
- Data Collection- All subsequent data will be collected and reviewed retrospectively. The following information needs to be submitted for each plan:
 - Full CT dataset
 - RS, RP and RD DICOM file (please note that the dose should be exported separately for the nodal and whole breast/chest wall volumes)
 - In case of a photon boost the dose cube for the boost should be exported and submitted separately as well.
 - Completed plan assessment form in electronic format

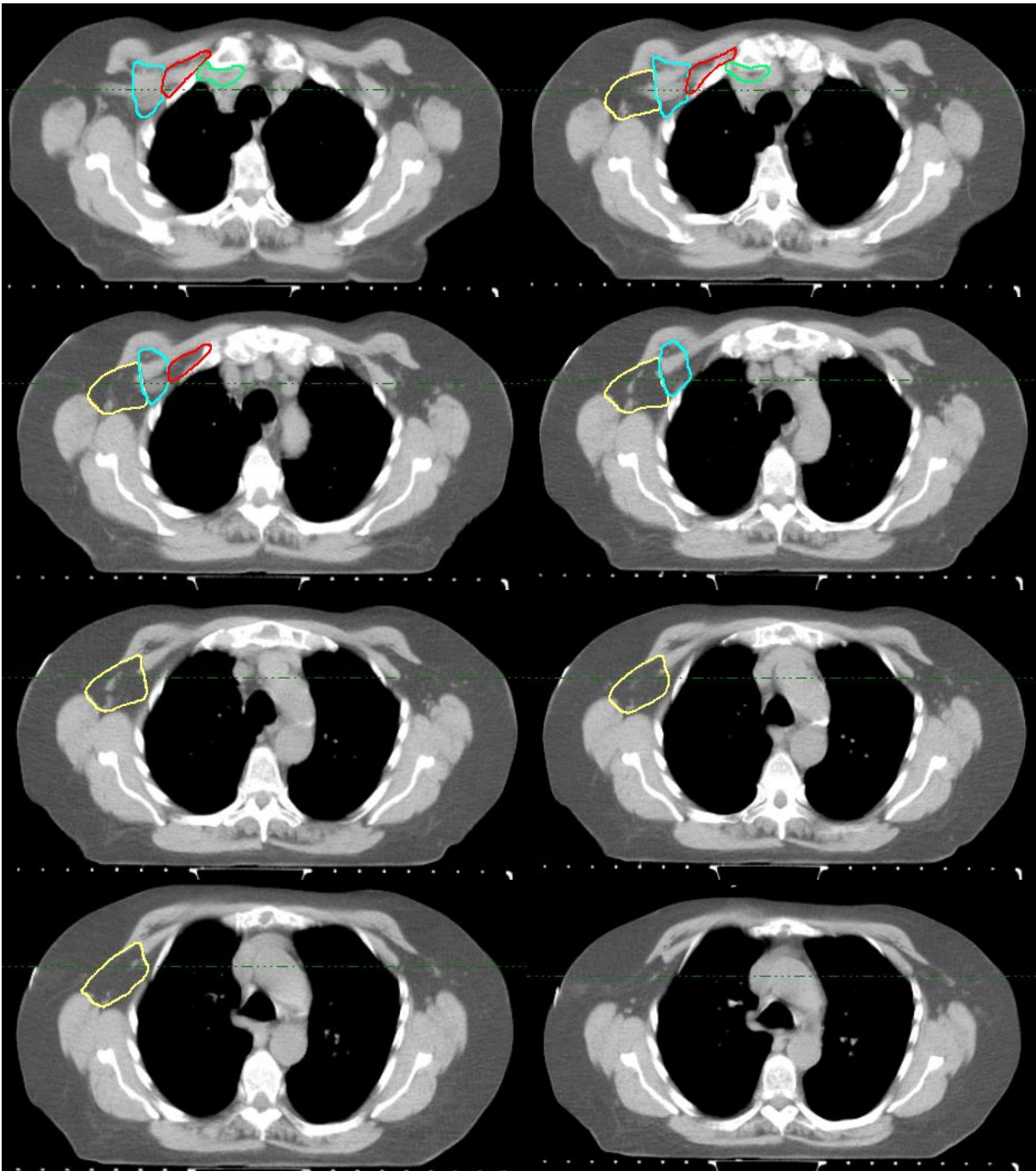
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3. Hall WH, Guiou M, Lee NY, Dublin A, Narayan S, Vijayakumar S, Purdy JA, Chen AM. Development and validation of standardized method for contouring the brachial plexus: preliminary dosimetric analysis among patients treated with IMRT for head-and-neck cancer. Int. J. Radiation Oncology Biol. Phys., Vol. 72, No. 5, pp. 1362–1367, 2008.
4. Elizabeth A. Miles, Karen Venables, Peter J. Hoskin, Edwin G.A. Aird. Dosimetry and field matching for radiotherapy to the breast and supraclavicular fossa. Radiotherapy and Oncology 91 (2009) 42–48.
5. International Commission on Radiation Units and Measurements. Prescribing, recording, and reporting photon beam therapy. ICRU report. 1999, Bethesda, Md.: International Commission on Radiation Units and Measurements.

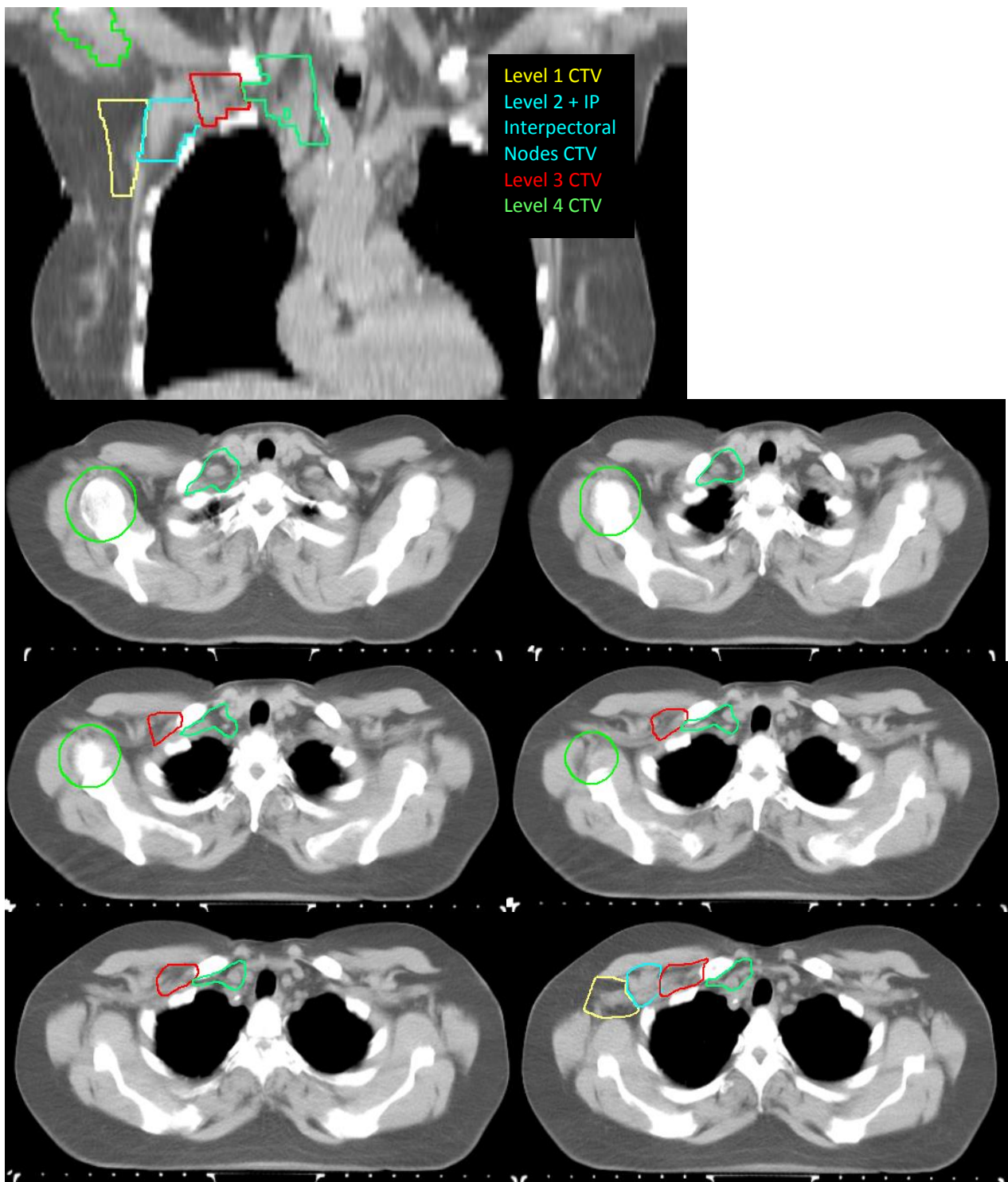
Appendix 1: Outlining examples

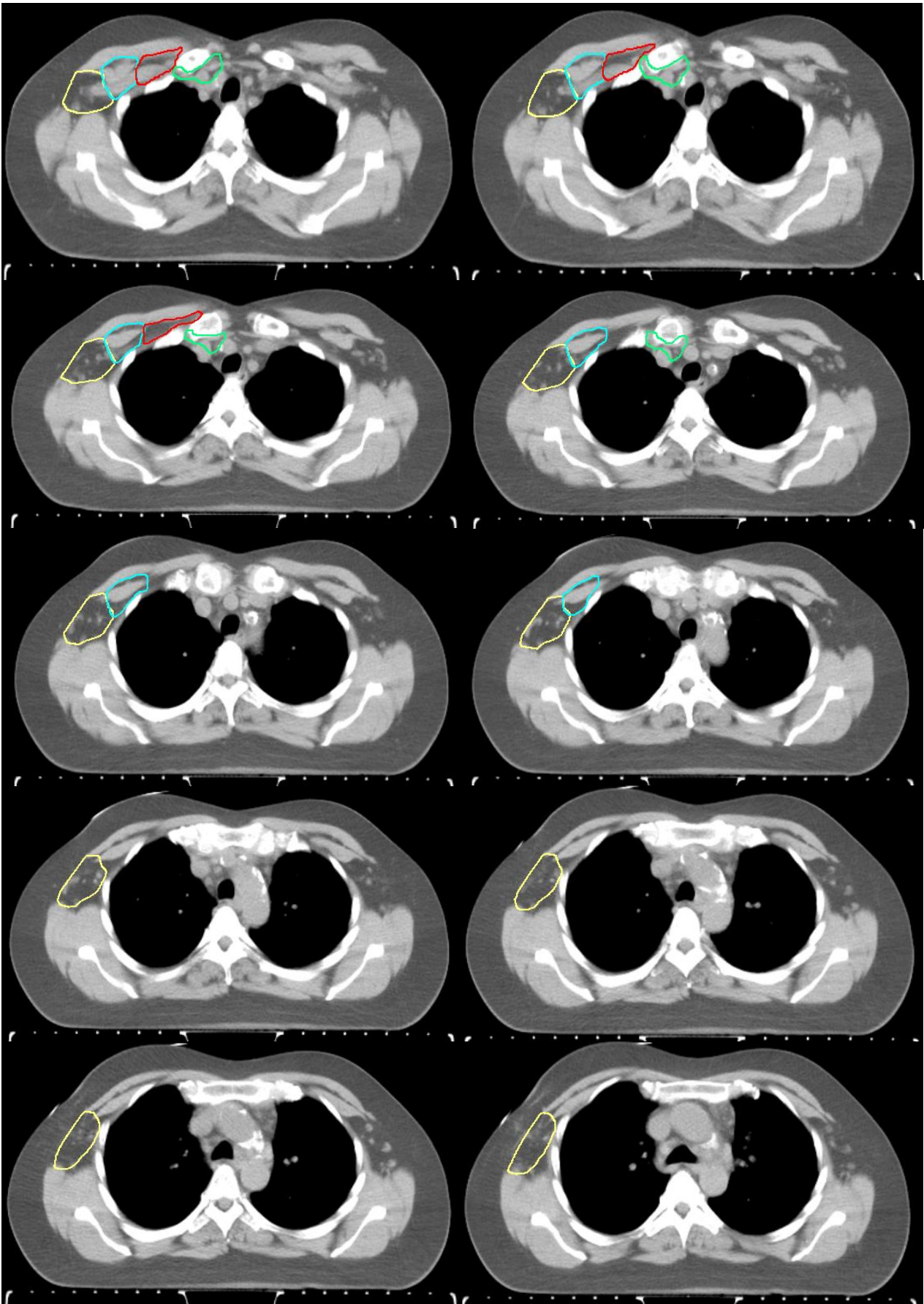
Outlining of the nodal CTVs – example 1





Outlining of the nodal CTVs – example 2





Outlining of the brachial plexus

