



ESTRO consensus guidelines

ESTRO consensus guideline on target volume delineation for elective radiation therapy of early stage breast cancer



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ABSTRACT

Background and purpose: Delineation of clinical target volumes (CTVs) is a weak link in radiation therapy (RT), and large inter-observer variation is seen in breast cancer patients. Several guidelines have been proposed, but most result in larger CTVs than based on conventional simulator-based RT. The aim was to develop a delineation guideline obtained by consensus between a broad European group of radiation oncologists.

Material and methods: During ESTRO teaching courses on breast cancer, teachers sought consensus on delineation of CTV through dialogue based on cases. One teacher delineated CTV on CT scans of 2 patients, followed by discussion and adaptation of the delineation. The consensus established between teachers was sent to other teams working in the same field, both locally and on a national level, for their input. This was followed by developing a broad consensus based on discussions.

Results: Borders of the CTV encompassing a 5 mm margin around the large veins, running through the regional lymph node levels were agreed, and for the breast/thoracic wall other vessels were pointed out to guide delineation, with comments on margins for patients with advanced breast cancer.

Conclusion: The ESTRO consensus on CTV for elective RT of breast cancer, endorsed by a broad base of the radiation oncology community, is presented to improve consistency.

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Elective radiation therapy (RT) of early stage breast cancer has proven to be very effective in lowering the risk of recurrences and improving overall survival [1], and it is therefore offered to many patients in the postoperative setting. However, there is also treatment-related morbidity, some relatively frequent and related to breast and shoulder [2,3], and others more seldom but potentially serious such as heart disease and secondary cancer development [4,5]. The risk of local recurrence has progressively decreased

over the last decades [6], while overall survival of breast cancer patients improved considerably [7]. It is therefore increasingly important to provide optimal RT to the patients to obtain a maximal effect at the lowest risk of late morbidity.

During the last decade a transition from 2D to 3D RT planning in early stage breast cancer has taken place in most European countries. In the 2D era bony landmarks were used to design RT fields, and it was difficult to individualise the field planning with respect to e.g. the heart because soft tissues were poorly visualised and displayed in a planar simulator-based projection only. Since then, the complexity of RT has increased gradually from just a few large fields to forward-planned field-in-field and even fully computerised intensity

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modulated radiotherapy (IMRT). With these approaches now used in most European clinics, it is possible to shape the fields closely around the target volumes with steep dose gradients between the CTV and the organs at risk (OAR) and to deliver a homogeneous dose distribution, reducing side effects and improving cosmetic outcome and the quality of life of patients [8]. In general, multiple equi-spaced axial fields are not recommended for breast RT, because this technique results in a low dose to a large volume of the body including the OAR [6]. Other advanced techniques are also being introduced quite rapidly, for example the simultaneous integrated boost to the primary tumour bed [9], and respiratory controlled techniques in left-sided patients [10]. Moreover, highly individualised treatment techniques can be required for individual patients based on anatomical variations that lead to a suboptimal dose distribution with standard treatment planning. This increasing complexity in the field of breast cancer RT emphasises the need for optimising the consistency and reproducibility in treatment planning, also to ensure comparability of treatment outcome among departments.

Currently, target volume delineation can be considered as the weakest part of the quality chain in RT. A large inter-observer variation is seen in delineation of regional lymph nodes, breast and thoracic wall. To minimise this, several guidelines for target volume delineation in early breast cancer [11–18] have been published. Atlases for delineating the heart have also been proposed [19,20], and recently software has been developed for autosegmentation of target volumes to support RT planning [21,22]. However, most of these guidelines, if applied as described, result in larger treated volumes than treated with conventional simulator-based RT. This can be explained in part by the use of the same fixed bony landmarks as used for simulator-based treatment set-up, followed by the addition of margins from CTV to PTV and to the field borders. An increase in treated volume should be avoided as no clinical reason for this exists and as this might lead to an increase in the dose to OAR [23]. Furthermore the use of systemic treatment has increased considerably over the last decade, and this may also have implications for the risk of radiation-related morbidity [3]. Since the first ESTRO teaching course on multidisciplinary management of breast cancer in 2009, target volume delineation has been practised and discussed in hands-on workshops, and during the five consecutive live courses as well as contouring exercises at congresses and online, the teachers from four countries (DK, ESP, F and NL) continued to work towards a European consensus on delineation guidelines for the clinical target volumes (CTVs) for elective lymph node areas, the breast and the thoracic wall in early stage breast cancer. The consensus has been sent to several colleagues active in treating early breast cancer, both in Europe and abroad, for further discussion, fine tuning and agreement. We now present hereby the final consensus guideline including the outcome of discussions held with radiation oncology specialists dedicated to the care of breast cancer patients from all over the world.

Materials and methods

One of the teachers of the ESTRO course (PP) started with delineating relevant CTV on non-contrast-enhanced computer tomography (CT) scans of two typical patients treated with breast conserving surgery and mastectomy for early breast cancer and scanned in supine treatment position, i.e. the patients were positioned on a breast-board inclined at 12.5–15° with both arms abducted around 120°. The head was positioned straight with the chin slightly upwards, avoiding skin folds at the level of the lower neck. This guideline does not describe the special issues regarding patients treated in prone position, because the anatomy is significantly different in that position.

Before CT scanning two circles of radio-opaque wires were placed around the breast representing the palpable/visible CTV

breast (inner circle) and the provisional field borders (outer circle) to aid in target volume delineation. The scans were made under free breathing and with 2.5 mm thick sections. It was decided to use nomenclature according to Santanam et al. [24], thus the suffix *n* indicates nodal areas and *p* indicates (post-operative) primary tumour volumes. The three other teachers commented, and specific borders were discussed during ESTRO courses and at telephone conferences, also using ESTRO's FALCON platform for volume delineation. Based on this, PP and BVO adapted the delineations. Most of the discussions among teachers were devoted to finding a compromise between real anatomical borders and practical clinical borders to prevent an increase in size of the RT fields compared to conventional RT fields. For example, although the anatomical medial border of the supraclavicular region was considered to be 5 mm around the veins, the carotid artery was excluded and no margin around the jugular vein was added, since a Danish analysis has shown a very limited number of regional recurrences, and those that appeared were within the high dose zone [23]. In addition, the guidelines were discussed with the Belgium group [25], and further adaptations were made with more attention paid to the vessels and less to bony structures. A suggestion for an anatomical overview of vessels is to look at <http://www.ikonet.com/en/health/virtual-human-body/virtualhumanbody.php>.

Results

Consensus was obtained for delineation of the CTV_n for elective irradiation of all regional lymph node areas, including axillae level 1–3, the supraclavicular region, which we recommend to be named level 4, the interpectoral (Rotter) nodes, the internal mammary nodes (IMN) region, the breast and the thoracic wall after mastectomy. In Table 1 the consensus boundaries of the lymph node areas are provided. We highlight that these guidelines are not intended for cases with locally advanced disease, since delineation in these cases should be highly individualised with the proposed guidelines serving as a base on which the CTV can be individually adapted. Where appropriate, we assume a slice thickness of the planning CT-scan of 2–3 mm.

Axilla level 1: CTV_n_L1

In general, visualisation of axillary level 1 is influenced by surgical scarring after ALND or sentinel lymph node biopsy (SLNB), which usually should be included in the CTV_n_L1. The medial border of CTV_n_L1 matches the lateral border of CTV_n_L2 and more caudally it is limited by the thoracic wall. Cranially, the axillary vein should be included with a margin of 5 mm in the surrounding fatty tissue often corresponding to the level where the axillary artery crosses the lateral edge of pectoralis minor muscle. It should be mentioned that the axillary vessels are often difficult to identify in level 1. To avoid inclusion of the scapula-humeral joint and the connective tissues around this joint, the craniolateral border of CTV_n_L1 is to be delineated up to 1 cm inferior and medial to the humeral head to avoid inclusion of this joint in the field, as in conventional RT planning. To facilitate this a Planning Risk Volume (PRV) 1 cm around the humeral head may be delineated (Fig. 1). More caudally, the lateral border is limited by an imaginary line between the lateral edge of the pectoralis major muscle and the antero-lateral edge of the deltoid muscle. Caudal to the deltoid muscle, the latissimus dorsi muscle defines the dorsal end of the imaginary line to the major pectoral muscle, thus excluding the subcutaneous fatty tissue lateral to this line from the CTV. The caudal limit in the mid-axillary line is considered around the level of costae 4–5. The cranio-posterior edge of CTV_n_L1 is limited by the ventral edge of the subscapular and

Table 1

ESTRO delineation guidelines for the CTV of lymph node regions, breast and postmastectomy thoracic wall for elective irradiation in breast cancer (see figures).

Borders per region	Axilla level 1 CTVn_L1	Axilla level 2 CTVn_L2	Axilla level 3 CTVn_L3	Lymph node level 4 CTVn_L4	Internal mammary chain CTVn_IMN	Interpectoral nodes CTVn_interpectoralis	Residual breast CTVp_breast	Thoracic wall CTVp_thoracic wall
Cranial	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	Includes the cranial extent of the axillary artery (i.e. 5 mm cranial of axillary vein)	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)	Caudal limit of CTVn_L4	Includes the cranial extent of the axillary artery (i.e. 5 mm cranial of axillary vein)	Upper border of palpable/visible breast tissue; maximally up to the inferior edge of the sterno-clavicular joint	Guided by palpable/visible signs; if appropriate guided by the contralateral breast; maximally up to the inferior edge of the sterno-clavicular joint
Caudal	To the level of rib 4 – 5, taking also into account the visible effects of the sentinel lymph node biopsy	The caudal border of the minor pectoral muscle. If appropriate: top of surgical ALND	5 mm caudal to the subclavian vein. If appropriate: top of surgical ALND	Includes the subclavian vein with 5 mm margin, thus connecting to the cranial border of CTVn_IMN	Cranial side of the 4th rib (in selected cases 5th rib, see text)	Level 2's caudal limit	Most caudal CT slice with visible breast	Guided by palpable/visible signs; if appropriate guided by the contralateral breast
Ventral	Pectoralis major & minor muscles	Minor pectoral muscle	Major pectoral muscle	Sternocleidomastoid muscle, dorsal edge of the clavicle	Ventral limit of the vascular area Pleura	Major pectoral muscle	5 mm under skin surface	5 mm under skin surface
Dorsal	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	Up to 5 mm dorsal of axillary vein or to costae and intercostal muscles	Up to 5 mm dorsal of subclavian vein or to costae and intercostal muscles	Pleura		Minor pectoral muscle	Major pectoral muscle or costae and intercostal muscles where no muscle	Major pectoral muscle or costae and intercostal muscles where no muscle
Medial	Level 2, the interpectoral level and the thoracic wall	Medial edge of minor pectoral muscle	Junction of subclavian and internal jugular veins – >level 4	Including the jugular vein without margin; excluding the thyroid gland and the common carotid artery	5 mm from the internal mammary vein (artery in cranial part up to and including first intercostal space)	Medial edge of minor pectoral muscle	Lateral to the medial perforating mammarian vessels; maximally to the edge of the sternal bone	Guided by palpable/visible signs; if appropriate guided by the contralateral breast
Lateral	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	Lateral edge of minor pectoral muscle	Medial side of the minor pectoral muscle	Includes the anterior scalene muscles and connects to the medial border of CTVn_L3	5 mm from the internal mammary vein (artery in cranial part up to and including first intercostal space)	Lateral edge of minor pectoral muscle	Lateral breast fold; anterior to the lateral thoracic artery	Guided by palpable/visible signs; if appropriate guided by the contralateral breast. Usually anterior to the mid-axillary line

ALND = axillary lymph node dissection.

deltoid muscles excluding the thoracodorsal artery and vein, which drain the back, and more caudally a horizontal line from the ventral edge of the latissimus dorsi muscle to the intercostal muscles is the dorsal limit.

Axilla level 2: CTVn_L2

This volume is located dorsal to the minor pectoral muscle. Medially the volume extends to the medial border of the minor pectoral muscle, and the cranial border includes the axillary artery

that is positioned cranial to the vein, preferably with 1 extra slice for partial volume effect. The dorsal limit extends to a 5 mm security margin dorsal to the axillary vein into the surrounding fatty tissue, generally corresponding with the thoracic wall (ribs and intercostal muscles). The lateral border is the lateral edge of the minor pectoral muscle. The caudal limit is the caudal border of the minor pectoral muscle, where artefacts may be visible after axillary lymph node dissection. The caudal border may therefore in these cases be modified to exclude the surgical bed from the Level 2 volume.

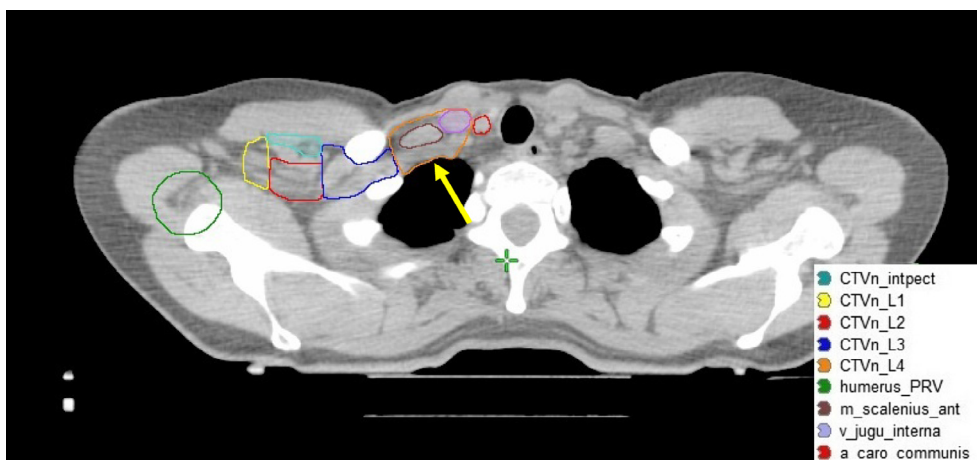


Fig. 1. Overview of CTVn_L1, CTVn_L2, the CTVn_interpectoralis, CTVn_L3, and CTVn_L4 at the midlevel of the subclavian arch (yellow arrow). Notice, in green the PRV delineated 1 cm around the humeral head to help delineation of the lateral border of CTVn_L1.

The interpectoral lymph nodes

These lymph nodes are also known as the Rotter lymph nodes, and are located ventral to the minor pectoral muscle and dorsal to the major pectoral muscle, while the cranial, caudal, lateral and medial limits largely reflect the limits of CTVn_L2.

Axilla level 3: CTVn_L3

This volume is often named the infraclavicular volume, and it is positioned medially to the minor pectoral muscle and CTVn_L2. The medial limit is the clavicle and the junction between the subclavian and internal jugular veins. The subclavian vein is located caudal to the artery, so the cranial border includes the artery with an extra slice due to partial volume effect and thus follows the cranial border of CTVn_L2 in the medial direction and connects to the caudal limit of CTVn_L4. At the most medial part, the cranial border is formed by the clavicle. The caudal limit is an extension of 5 mm in the fatty tissue caudal to the subclavian vein. The volume is positioned dorsal to the major pectoral muscle. The dorsal limit is 5 mm dorsal to the subclavian vessels (extension only into the fatty tissue), also limited by the ribs and intercostal muscles.

Lymph node level 4: CTVn_L4

This volume is usually named the supraclavicular volume, however, since the definition of the supraclavicular CTV for breast cancer is not the same as it is for example for head and neck cancer, we decided to name this volume CTVn_L4, which also reflects the continuum of the lymphatic drainage pattern of breast cancer. Medially the internal jugular vein is included without a margin, thus excluding the common carotid artery and the thyroid gland. The cranial edge of CTVn_L4 is at the cranial level of the subclavian artery arch, which is always positioned cranial to the subclavian vein. In this way, a margin of 5 mm cranial to the subclavian vein is achieved. Considering the partial volume effect and slice thickness of the CT scan, the most cranial delineation can be made 1 slice cranial to the subclavian arch. It may be helpful identifying the cranial border of this volume not only by following the subclavian vessels in the sagittal plane, but also in the coronal plane (Fig. 2). Vento-laterally, the limit is the dorsal side of the sternocleidomastoid and sternothyroid muscles and the clavicle. The most lateral extension includes the connective tissue between the lateral border of the anterior scalene muscle and the clavicle and connects with the medial border of CTVn_L3. The caudal edge

of this volume includes the subclavian vein with 5 mm and connects to the CTVn_IMN. The dorsal border is the pleura.

CTVn_IMN

This volume includes the lymph nodes alongside the internal thoracic veins, which are always positioned medially to the corresponding arteries. On the right side, the internal thoracic vein drains into the brachiocephalic vein, while the internal thoracic artery originates from the subclavian artery, with up to 1–2 cm distance in cranio-caudal direction between these vessels dorsal to the clavicular head. On the left side the internal thoracic vessels are connected to the subclavian artery and the brachiocephalic vein with less distance in-between. In the most cranial part, where only the artery is present, a margin of 5 mm is added to the artery. In order to achieve a smooth connection between the cranial and caudal part of the CTVn_IMN it is recommended to include the internal thoracic artery with 5 mm margin in the target up to 1 cm caudal of the point where the vein drains into the brachiocephalic vein. The cranial border is the caudal border of CTVn_L4, thus the most cranial part of this volume is delineated 5 mm around the internal thoracic artery. The caudal limit is usually the cranial side of the 4th rib but might be prolonged with one more intercostal space depending on the protocol. The medial limit is 5 mm medially to the vein or the sternum, whatever is closest,



Fig. 2. Illustration of the subclavian arch passing through the volume of CTVn_L4. It may be very helpful to identify the cranial level of CTVn_L4 as 1 CT slice cranial to the subclavian arch identified in the coronal plane.

the dorsal limit is the pleura, the ventral limit is an extension of 5 mm ventral of the vessels in the fatty tissue, and the lateral limit is 5 mm lateral to the vein.

CTVp_{breast}

This target volume includes the total glandular breast tissue, whose borders are often not clearly visible. To facilitate delineation, radio-opaque markers may be placed around the breast for CT-scanning, keeping in mind that these markers do not necessarily represent the true borders of the CTVp_{breast}. The dorsal border of the CTVp_{breast} is the ventral side of the major pectoral muscle and where that is not present the exterior side of the ribs and intercostal muscles. However, at the caudal part of the breast the dorsal border can be adjusted in ventro/ventrolateral direction – in particular in obese patients with a thick subcutaneous tissue layer – since this rather represents subcutaneous fat extending from the abdominal wall which is not part of the CTV. This can decrease the dose to the heart in left-sided cases (Fig. 3A). The ventral border is 5 mm under the skin surface except in cases with T4b, c and d cancer, where a full radiation dose up to the skin is advised, which can be obtained by using a bolus. The cranial border extends usually maximally up to the level of the caudal edge of the sterno-clavicular joint, without this being a strict criterion. The caudal border is the lowest CT slice with breast shape still visible. The medial border extends maximally to the ipsilateral edge of the sternal bone, without this being a strict criterion especially in the cases of ptotic breasts. Moreover, even in non-IV-contrast enhanced CT scans, it is usually possible to identify in some CT slices the medial mammary branches originating from the internal thoracic artery, and the breast glandular tissue is positioned lateral to these vessels – allowing for a reduction in the medial extension of the CTVp (Fig. 3B). At the lateral border, the breast tissue may produce a helpful – for delineation – fold, but in particular in obese patients it may be very difficult to define this border clearly. Here again help is provided from the vessels, since it is usually possible to identify the lateral thoracic artery from which the lateral part of the breast is nourished, and the CTVp_{breast} should be delineated ventral/medial to this vessel (Fig. 3C). Irrespective of the position of the primary tumour bed in the breast, care should be taken that the CTVp_{breast} encompasses the primary tumour bed, including relevant margins around.

CTVp_{thoracic wall}

In mastectomy patients, radio-opaque wires should be positioned around the –imaginary – original site of the breast and also corresponding to the mastectomy scar. While the position of the contra-lateral breast can be helpful for this if both arms are symmetrically elevated, in general the surface of the CTVp_{thoracic wall} is reduced by the surgical procedure following the pulling on adjacent skin and subcutaneous tissue to close the defect after removal of the breast. Therefore, careful palpation of the thoracic wall while positioning the radio-opaque markers and the position of the mastectomy scar should be used as well. In some countries, e.g. Denmark, it is standard to apply a 3 mm bolus alongside the mastectomy scar extending a total of 6 cm in cranio-caudal direction (DBCG consensus). This is to achieve a full radiation dose in the skin to avoid skin recurrences. In general, the boundaries of the CTVp_{thoracic wall} are similar to those of the CTVp_{breast} as described above. In slim patients, the thoracic wall may be so thin that the CTV_{thoracic wall} disappears when cropping the volume 5 mm beneath the skin. In such cases a 5 mm bolus may be applied, and the CTVp_{thoracic wall} should be extended up to the level of the skin. Unless invasion was demonstrated (tumour stage T4a

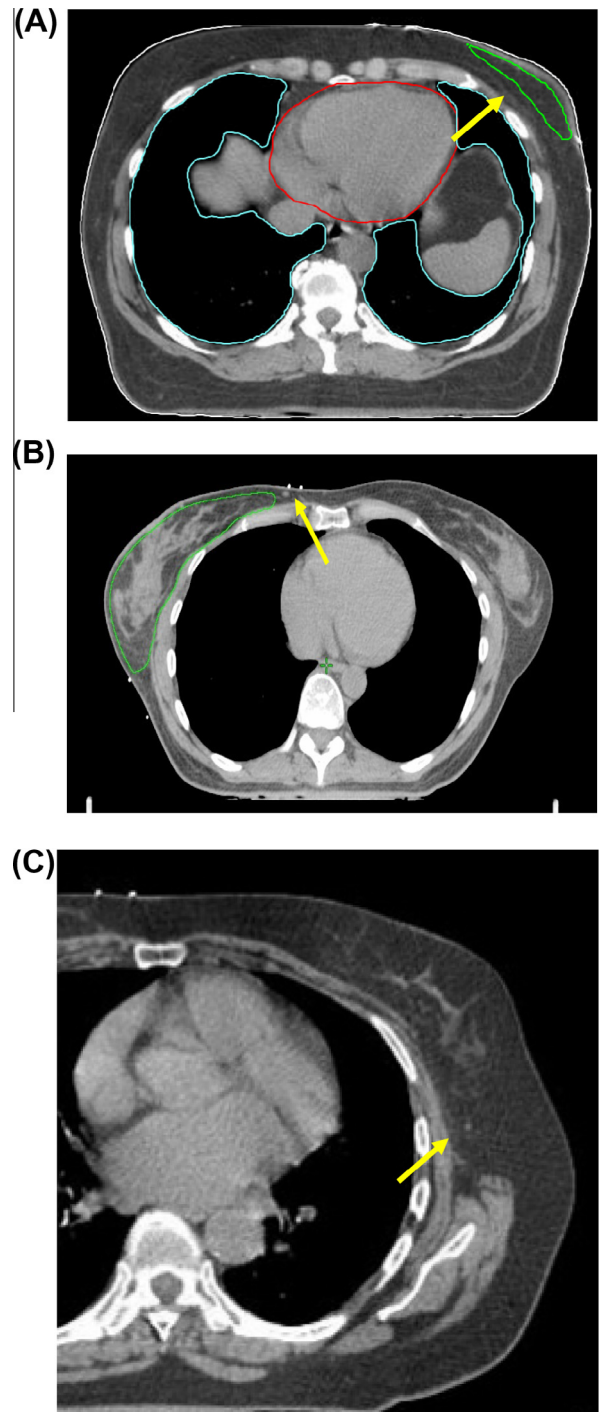


Fig. 3. (A) In relatively obese patients the CTVp_{breast} is positioned more ventrally in the caudal part of the breast due to fatty tissue. (B) It is often possible to identify medial mammary branches of the internal thoracic artery, and the CTVp_{breast} is positioned lateral to these vessels. (C) Arrow points at the lateral thoracic artery.

and T4c), there is no reason for routinely including the major pectoral muscle and the ribs in the CTVp_{thoracic wall}.

Overview of delineations

After completion of delineating all relevant target volumes, it is often helpful to look at all together in a 3D (rotatable) window to assure that the volumes are interconnected. To illustrate this, the overview of the ESTRO consensus delineations is shown in Fig. 4.

The DICOM files can be downloaded for free from <https://estro.box.com/s/5n3qbn6z3jpbcds63v3wmh4ga3xvwtuw> (Thoracic Wall Left: Guidelines 2014) and <https://estro.box.com/s/wzetm8r-md4tc09icowj1uzoinur02o1z> (Breast Right: Guidelines 2014).

Discussion

The ESTRO consensus on target volume delineation in early breast cancer provides guidelines for CTV for elective RT. It can also be used as a base for the individualised volume delineation for patients with locoregionally advanced disease. We repeat our strong recommendation that there is no reason to enlarge the radiation fields beyond those obtained with conventional simulator based treatment set-up. In a single-institution Danish study on the localisation of regional recurrences after regional RT over a 13 year period it is documented that the majority of regional recurrences occur in-field, thus not due to too small RT fields [23].

Since the CTVs are drawn on slices from a CT scan with a certain thickness, we recommend to enlarge the CTV with 1 slice in cranio-caudal direction to compensate for the partial volume effect. Therefore, we recommend a maximum slice thickness of 2–3 mm in order not to enlarge the field borders too much.

No consensus on definition of the primary tumour bed is proposed. For this, we refer to an earlier publication by Boersma et al. [26] and the ongoing work to obtain a consensus for APBI within the GEC-ESTRO group. The resulting ESTRO guideline is quite similar to the recently published Danish national guideline [18] and to the PROCAB consensus [25].

In Table 1 borders are listed for each CTV, however, the borders are not to be considered exact within mms, firstly because it is important to recognise that the lymph node volumes interconnect to each other to reflect the lymphatic drainage system and secondly because the extension of the CTV around the vessels can only be into the fatty tissue and evidently not into muscles or bony structures. When defining the target volumes as in Table 1, areas emerge where radiation dose is usually given but not actually prescribed. This is the case for example between the cranial border of CTVp_breast and the caudal border of the CTVn_L2–L3–L4 in cases with no indication for RT of CTVn_L1 (Fig. 4A). Indeed, if treatment planning is based solely on these delineated CTVs, a gap may exist between the irradiated volume of the breast/thoracic wall and the lymph node regions. This prompted the group behind the DBCG guidelines to define CTVn_interpectoral lymph nodes as a relatively large volume, thus assuring that no “cold” spots were seen when planning RT [18]. As this is conceptually not correct, we anticipate that in the future “cold” spots are to be accepted in between the different irradiated volumes. Until then, we suggest to adapt the fields thus assuring radiation dose also in the “cold” spots.

For some of the volumes in Table 1 additional comments should be added to the definition:

- As the lymph nodes follow the lymphatic vessels that are mainly located around the veins, the borders are as much as possible related to the position of the veins rather than to the bony anatomy.
- One of the major differences between the ESTRO consensus compared to for example the guidelines proposed by Dijkema and from Institute Curie, Paris, is the dorsal border of CTVn_L1 and CTVn_L2, which to a large extent defines the depth of the target volumes [12,17]. Therefore, this dorsal border is very important for the field arrangement and steepness of the tangential fields, with a subsequent larger volume of lung irradiated with a more dorsal border. Based on the low rate of recurrences located in the dorsal part of CTVn_L1 and CTVn_L2 after conventional RT, where a full dose is not obtained, it was decided to modify this border in ventral direction [23].

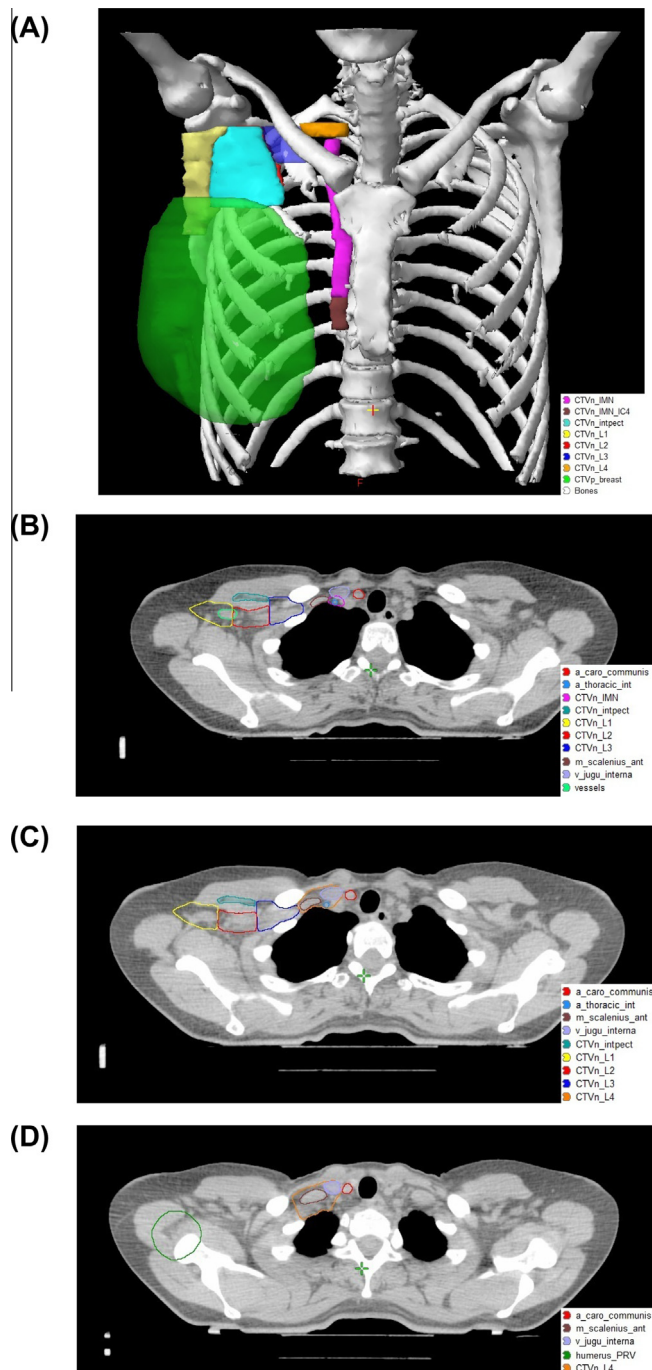


Fig. 4. (A) 3D overview of the lymph node volumes. Notice, that all volumes are interconnected. The CTVn_IMN has been delineated to include intercostal space IV also (brown colour). (B) Overview of the lymph node areas at the cranial level of CTVn_IMN. (C) Overview of the lymph node areas at the caudal border of CTVn_L4. (D) Overview of the lymph node areas at the cranial level of CTVn_L4.

- Another major difference between this consensus and other previously published guidelines is the position of the cranial border of CTVn_L4. According to the ESTRO consensus this border is one CT slice cranial to the cranial border of the subclavian artery, in harmony with the principle that the lymph nodes follow the veins. The clinical experience, also supported by the Danish study [23], is that the localisation of supraclavicular nodal relapse is most often in the angle between the cranial border of the clavicle and the dorsal edge of the sternocleidomastoid muscle (in patients previously treated with regional

RT including the supraclavicular fossa). In cases with locally advanced breast cancer (for example if there are pathological nodes in level 3) it may be relevant to modify the cranial border of CTVn_L4 to a more cranial position, thereby accounting for lymphatic spread beyond the first lymph node levels. In such cases we suggest to add a 10–20 mm margin to the pathological node to define the CTV as also suggested in the recent guidelines for head and neck cancer RT [27].

- Another issue deserving special attention is the part of CTVn_IMN dorsal to the sterno-clavicular joint, where a small part of this volume is usually not included in conventional RT field planning due to its deep location. If this part of the CTVn_IMN was to be fully included in the RT fields it might, depending on the individual anatomy and the technique used, cause much increase in the dose to the ipsilateral lung. Moreover, it is uncertain whether this most cranial part of the CTVn_IMN is clinically relevant, since the internal mammary veins drain into the brachiocephalic veins 1–2 cm caudal to the corresponding arteries, thus there may be no lymph nodes in this “gap”. In the EORTC and DBCG IMN studies the CTVn_IMN dorsal to the sternoclavicular joint was often not treated to the full dose. In the DBCG IMN study the radiation dose in CTVn_IMN dorsal to the sterno-clavicular joint at the level of costa 1 was evaluated in 10 consecutive patients, where the CTVn_IMN was intended to be treated. At the ventral and dorsal edges of the CTVn_IMN the doses were 80–100% and 10–20%, respectively (Thorsen LBJ, personal communication). The caudal limit of the CTVn_IMN remains uncertain, since radiotherapy to the first 3 intercostal spaces was advised in the EORTC study, unless with an inner lower located tumour [28], and the first 4 intercostal spaces were included in the DBCG study [29]. We suggest the following, like in the last amendment of the EORTC trial: the target volume always includes the IMN nodes in the first 3 intercostal spaces; in medial lower quadrant lesions the target volume can be extended to include the 4th intercostal space but depends also on the specific anatomy of the individual patient.
- Finally, this ESTRO consensus advocates the supraclavicular lymph node volume to be named as CTVn_L4 reflecting the continuum of lymph nodes receiving drainage from the breast, thereby also highlighting that only the lowest part of the supraclavicular lymph node region should be considered as part of the CTV in elective LN irradiation in breast cancer.

In the case of advanced breast cancer, the ESTRO guidelines can be used as a starting point with individual adaptation based on the extent of the primary tumour and the lymph node involvement. IV-contrast enhanced CT scans are helpful for learning purposes when defining the targets, however, in daily routine it is not considered necessary. A normal anatomy atlas should be available as it often turns out to be very helpful. We stress the importance of adding a margin to the CTV to obtain a PTV for planning purposes. Specific advice on the size of the PTV margins cannot be made, since they should be based on actual measurements of set-up performance.

Approval of an RT plan is an important part of the multidisciplinary treatment of early stage breast cancer, thus the full picture of the patient should be considered in order to balance the compromises when evaluating and approving the RT plan based on the dose distribution.

While looking for international endorsement of the anatomy-based guidelines, we had an exchange of thoughts with representatives of RTOG. Published in 2009, the RTOG Breast Cancer Atlas and its consensus definitions are the foundation for all of their contemporary breast cancer clinical trials, both completed and ongoing. Therefore, representatives of RTOG preferred not to change this

atlas now. If pre-set dose constraints cannot be met, other treatment techniques might be used or, depending on the estimated risks of shielding part of the target volume, an underdose of part of the CTV/PTV might be accepted. It is however important to bear in mind that the patient may have a significantly higher benefit from the RT than harm as pointed out in the Danish study on effect from RT of the IMN [30]. In that study the number needed to treat to avoid one death at seven years after IMN RT was 33 patients. In “the worst case” scenario with optimal dose coverage of the IMN (intercostal spaces 1–4) but without respecting heart constraints in a left-sided breast cancer patient 50 years old and with no heart risk factors, the number needed to harm to cause 1 death from ischaemic heart disease 10 years after RT was estimated 3333 patients and 30 years after RT 143 patients. Thus refraining from IMN RT may spare some ischaemic heart deaths, but the overall survival benefit from IMN RT outweigh the cost of heart death.

The goal with this ESTRO consensus is to provide a useful and reproducible guideline for target volume delineation for RT for early breast cancer. The guidelines will continue to be used during ESTRO teaching courses and other delineation exercises, and hopefully they will be followed for the benefit of our patients.

Conflicts of interest

None.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.radonc.2014.11.030>.

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