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FULL PAPER

Radiological findings on irradiation-CT in patients with non metastatic breast cancer

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Objective: The aim of this study was to evaluate the number of incidental findings on native CT treatment-planning scans for radiation in breast cancer patients.

Methods: The treatment-planning scans of 382 patients with non-metastatic breast cancer were retrospectively analyzed for additional findings. The planning scan area covered the entire thorax and the upper part of the abdomen. Incidental findings were classified according to their clinical relevance.

Results: Overall 892 incidental findings were detected in the CT treatment-planning scans (mean 2.34 findings per patient). Only a small proportion of patients ($n = 63$, 16.4%) had no finding. Most findings were located in the thorax (683, 76.57%), and 209 findings (23.43%) were abdominal. 79 findings (8.87%) were of

major clinical relevance, 232 findings (26.01%) were of moderate clinical relevance and 580 findings (65.02%) were of minor clinical relevance. Most clinically relevant findings were in the thorax ($p = 0.006$). Abdominal findings were more of significantly minor clinical relevance ($p < 0.0001$).

Conclusion: Radiological findings are frequent in native CT treatment-planning scans for radiation of breast cancer patients. Therefore, the radiologist should use this performed sectional image to obtain additional information of the patient.

Advances in knowledge: Treatment-planning CT scans can show several radiological findings, namely 2.34 findings per patient. Major clinically relevant findings account for 8.87%.

INTRODUCTION

Radiation therapy planning CT (planning CT) is the foundation of modern radiotherapy; planning CTs are crucial for visualization of the therapeutic area and for optimal implementation of radiation therapy. Planning CTs facilitate the precise localization of treatment volumes, the optimization of dose distributions and the minimization of radiation exposure to radiation-sensitive organs.^{1–5}

Critical structures are efficiently identified on planning CTs, and their volumes in the irradiation range can be reliably determined. This method yields improved cancer control while reducing mortality.^{3,4}

Incidental findings are defined as findings unrelated to the scope of the ordered investigation.⁶ Lumberras et al⁷ published a widely known classification to categorize incidental findings according to their clinical relevance. Recently,

further classification systems for incidental findings have been published, underlining their clinical importance.^{8–12}

Several studies have described the competence of planning CTs in detection of unexpected clinical findings, such as metastases of the primary tumour or other concurrent malignant diseases.^{5,13,14}

In this context, planning CTs for breast cancer patients are of special interest.

Primary diagnostic procedures for breast cancer include clinical examination of the breast, mammography and ultrasound.¹⁵ Breast cancer staging is concluded by chest radiographs, skeletal scintigraphy and ultrasound examination of the liver.¹⁵

For most breast cancer patients, planning CTs are the only cross-sectional imaging procedure performed and thus

yield valuable additional information. Even if performed in low-dose technique, the diagnostic accuracy of CT is superior to chest radiography in the detection of pulmonary nodules.¹⁶

Despite the potential clinical impact of incidental findings on planning CTs in general, and for breast cancer patients in specific, there is a paucity of studies on this topic.

Therefore, the aim of our study was to evaluate clinical incidental findings on non-contrast-enhanced planning CTs for irradiation of non-metastatic breast cancer.

METHODS AND MATERIALS

Study population

The electronic database of the radiological department at the tertiary referral university hospital (Halle Saale, Germany) was retrospectively searched for planning CTs from 2010 to 2015. Electronic patient records were available for this period, and the same CT scanner was used for radiation planning scans.

Planning CTs were included if performed for patients with non-metastatic breast cancer, irrespective of gender (Figure 1). Patients were excluded if diagnosed with positive lymph node status.

The study was approved by the local ethics committee and received an informed consent waiver due to its retrospective design. The study was conducted in accordance with the Declaration of Helsinki.

CT technique

Planning CTs were performed with 120 kVp, 316–568 mAs and a layer thickness of 5 mm using a multilayer CT scanner (LightSpeed™ RT 16, GE Medical Systems, Milwaukee, WI).

Scan length reached from the upper thoracic aperture for the upper abdomen. All images were reconstructed with standard algorithms using a manufacturer-specific kernel (Kernel “Standard”, GE Medical Systems). Window values “middle” and “width” with 450/1500 were used for evaluation of bone structures: –250/1600 for evaluation of lung tissue and 56/342 for evaluation of soft tissue.

Owing to the retrospective design of the study, no reconstructions with a specific kernel for soft tissue or lung tissue were available. Comparably, further clarification of clinically relevant additional findings by other imaging methods or biopsy was not possible.

Figure 1. Acquisition of data for the study.

Incidental finding classification

Incidental findings were classified according to the system proposed by Lumbreras et al.⁷ In summary, three categories rank the findings according to their clinical relevance. Category 1 is labeled “major clinical relevance” with findings that might alter the patients’ clinical course, *i.e.* aortic aneurysms or tumours. Category 2 is labeled “moderate relevance” with findings where follow-up is sufficient, *i.e.* adrenal adenomas. Category 3 is labeled “minor clinical relevance” with findings not influencing the patients’ course, *i.e.* simple cysts.

Data acquisition and analysis

The following data were acquired: age and sex of the patients, histopathological classification and stage of breast cancers, localization and size of incidental findings.

Only non-osseous incidental findings were involved in the study.

All images were digitally analyzed on a picture archiving and communication system workstation (Centricity PACS; GE Medical Systems).

Planning CTs were analyzed by two independent readers (AS and DS) with 11 and 4 years’ radiological experience, respectively. Reader discrepancies were solved by consensus.

Full electronic patient record access was granted to ensure a realistic and generalizable reading scenario. Furthermore, the patient records were screened to ensure that incidental findings were unknown prior to planning CT scans.

For descriptive statistics, categorical variables are provided as number and percent. Fisher’s exact test was used to compare clinical relevance of thoracic and abdominal incidental findings. All statistical analyses were conducted using GraphPad Prism® v. 4 (GraphPad® Software Inc., La Jolla, CA). An alpha level of 0.05 was chosen for statistical significance. All provided *p*-values are two sided.

RESULTS

Study population

In total, 382 patients fulfilled the inclusion criteria. The study population comprised 380 (99.47%) females and 2 (0.52%) males with a mean age of 61 ± 10 years (range 33–88 years).

In addition to radiotherapy, 18 patients (3.4%) received neo-adjuvant chemotherapy. Tumour stage of included patients is provided in Table 1. Table 2 summarizes histological classification of tumors.

Incidental findings

A total of 892 incidental clinical findings were detected in the study population of 382 patients. The mean incidental clinical findings per patient were 2.34. In 63 patients (16.4%), no incidental clinical finding was diagnosed. Most of the findings were localized in the thorax ($n = 683$, 76.57%), abdominal incidental clinical findings were found in 209 cases (23.43%). Table 3 summarizes clinical incidental findings localization. Of 892 clinical incidental findings, 79 (8.87%) were of major clinical

Table 1. Tumour stage of included patients

Tumour stage	<i>n</i>	%
Ductal carcinoma <i>in situ</i>	85	22.25
pT1 N0 M0	191	50.00
pT2 N0 M0	50	13.08
pT3 N0 M0	1	0.26
pTx N0 M0	37	9.68
yT0 N0	13	3.4
yT1 N0	3	0.78
yT2 N0	2	0.52

relevance, 232 (26.01%) were of moderate clinical relevance and 580 (65.02%) were of minor clinical relevance (Figures 2–5).

Thoracic incidental clinical findings

The most frequent thoracic findings were regressive changes of the thyroid gland in 92 patients, pleura cicatrix in 85 patients, pleural capping in 64 patients and cardiomegaly in 60 patients.

Thoracic findings were of major clinical relevance in 73 cases (10.70%), moderate clinical relevance in 223 cases (32.70%) and of minor clinical relevance in 386 cases (56.60%).

Cardiomegaly was the most common major clinically relevant finding ($n = 60$). In seven cases, lung fibrosis was diagnosed. In three cases, there was unclear mediastinal lymphadenopathy.

Frequencies and clinical relevance of incidental findings of the thorax are summarized in Table 4.

Abdominal incidental clinical findings

Abdominal findings were axial hiatus hernias in 79 patients, cystic hepatic lesions in 66 patients and hepatic steatosis in 20 patients.

6 abdominal findings were of major clinical relevance (2.87%), 9 abdominal findings were of moderate clinical relevance (4.30%) and 194 abdominal findings were of minor clinical relevance (92.83%).

Clinically relevant findings comprised five nodules of the adrenal cortex, as well as one unclear focal hyperdensity of the liver.

Table 2. Histopathological tumour classification

Histopathological classification	<i>n</i>	%
Ductal	226	59.16
Ductal carcinoma <i>in situ</i>	85	22.25
Ductolobular	32	8.37
Lobular	20	5.23
Histopathology not available	12	3.14
Other	7	1.83

Table 3. Incidental findings localization

Localization	<i>n</i>	%
Pleura	168	18.83
Lung	152	17.04
Vessels	143	16.03
Mediastinum	114	12.78
Heart	109	12.22
Liver	102	11.43
Stomach	79	8.86
Kidney	8	0.90
Adrenal glands	4	0.45
Integument	2	0.22
Diaphragm	1	0.11
Pancreas	1	0.11
Spleen	9	1.0
Total	892	100

Table 5 details frequencies and clinical relevance of incidental findings of the abdomen.

Statistical analyses

The clinical significance of incidental findings varied by location.

Thoracic incidental findings were more often of major or moderate clinical relevance than abdominal findings. This observation reached statistical significance at the chosen alpha level ($p = 0.006$, $p < 0.001$, respectively).

DISCUSSION

Current diagnostic guidelines for breast cancer recommend anamnesis, clinical breast examination, ultrasound and mammography.¹⁵ Breast cancer diagnosis is confirmed by means of

Figure 2. Pulmonary lesion (arrow) as a clinically relevant finding.

Figure 3. Aneurysma of the aorta ascendens (arrow; major clinically relevant finding).

biopsy and histopathologically examination.¹⁵ MRI is not routinely performed in the diagnostic path of breast cancer evaluation.¹⁵ Clinical staging for breast cancer includes chest radiography, ultrasound of the liver and bone scintigraphy.¹⁵

For non-metastatic breast cancer patients, planning CT is therefore the only cross-sectional imaging modality. However, since these planning CTs are conducted for radiotherapy, they are not routinely read by radiologists.

This present study shows that a considerable proportion of incidental clinical findings can be obtained in planning CTs.

Moreover, in up to 11%, these findings were of high clinical relevance, potentially requiring further diagnostic and therapeutic measures, and ultimately influencing patient outcome.

Therefore, a deliberate reading of planning CTs with special attention on the thorax is crucial for optimal management of breast cancer patients.

Figure 4. Radiation scan showing a kidney stone (arrow) as a moderate clinically relevant finding.

Figure 5. Enlargement of the left adrenal gland (arrow; major clinically relevant finding).

Our findings are supported by earlier studies, reporting a considerable proportion of planning CTs with relevant clinical incidental findings.^{13,14,17,18}

In our study, a total of 892 clinical incidental findings were detected in 382 breast cancer patients, averaging at 2.34 findings per patient. A small number of patients without findings further support the accurate reading by two independent radiologists.

Most findings were localized in the thorax, which could be attributed to planning CT scanning range mainly covering thoracic regions. Only cranial parts of the abdomen were covered by planning CTs, which might explain the lower absolute number of abdominal findings.

However, the proportion of clinically relevant abdominal findings should be unbiased by this imaging method. Compared with abdominal findings, thoracic findings were more frequently clinically relevant or potentially relevant.

With 11% clinical incidental findings, our study is comparable to Rao et al¹⁸ and Kim et al¹⁷ reporting on 9% and 19.8% findings on planning CT for breast cancer patients.

Planning CTs for radiotherapy in breast cancer patients are routinely performed without contrast enhancement. In addition, planning CTs differ from diagnostics in layer thickness and patient positioning.¹⁷ Radiotherapy markers or immobilizing devices using planning CTs can produce artefacts and thus impair imaging evaluation.¹⁷

According to the literature, diagnostic accuracy of planning CTs can be improved by intravenous administration of contrast media.¹⁷ However, in our study, we demonstrated the diagnostic competency of non-contrast-enhanced planning CTs in the detection of clinically relevant findings. This is in agreement with another non-contrast-enhanced CT study on multiple myeloma patients.¹⁹

Table 4. Thoracic incidental findings

Finding	<i>n</i>	Percent of all thoracic findings	Clinical relevance (Lumbreras et al ⁷)
Cardiomegaly	60	8.78	Major
Lung fibrosis	7	1.02	Major
Mediastinal lymphadenopathy	3	0.44	Major
Aortic aneurysm	1	0.15	Major
Pleural nodule	1	0.15	Major
Pleural nodule	1	0.15	Major
Emphysema	52	7.61	Moderate
Coronary sclerosis	48	7.03	Moderate
Aortic ectasia	33	4.83	Moderate
Pulmonary nodule	24	3.51	Moderate
Pulmonary consolidation	23	3.36	Moderate
Aortic valve sclerosis	20	2.93	Moderate
Mitral valve sclerosis	11	1.61	Moderate
Pulmonary congestion	11	1.61	Moderate
Ectasia of the pulmonary trunk	1	0.15	Moderate
Solitary large thyroid nodule	1	0.15	Moderate
Goitre	92	13.47	Minor
Pleural cicatrix	85	12.45	Minor
Pleural capping	64	9.37	Minor
Elongation of the aorta	57	8.34	Minor
Pulmonary post-inflammatory changes	29	4.24	Minor
Pulmonary calcifications	17	2.49	Minor
Hilar calcifications	15	2.20	Minor
Pleural thickening	14	2.05	Minor
Thyroid calcification	5	0.73	Minor
Dilated right atrium	2	0.29	Minor
Pericardial calcification	2	0.29	Minor
Pleural calcification	2	0.29	Minor
Calcified oesophageal lymph node	1	0.15	Minor
Calcification of the diaphragm	1	0.15	Minor
Total	683	100	

CT slice thickness is crucial for the detection of clinical findings on planning CTs;¹⁷ for example, in CT scans with 5-mm slice thickness, minor lesions could be missed due to lower z-axis resolution than CT scans with 4-mm layer thickness.

In addition, detection of clinical findings on planning CTs might be influenced by patient population and the area of interest.⁷ Retrospective analyses have shown that more malignant findings were reported in patients with breast cancer than those with prostate cancer.⁷ In our study, no further malignant findings were reported, since only patients in early tumour stages without nodal involvement were excluded, thereby reducing the likelihood of metastatic disease. On the other hand, findings such as

pulmonary nodules found on planning CTs can be of great clinical relevance for further control CTs. Moreover, some findings might be of malignant character. For example, breast cancer metastases might present as liver cysts, and pulmonary nodules could reflect early stage lung cancer. Owing to the retrospective design of our study, dedicated follow-up of incidental findings was impossible. As of 2017, no patient presented to our tertiary hospital with cancers identified as incidental findings on planning CTs.

The high number of clinically relevant and potentially clinically relevant findings underscores the necessity for immediate, deliberate reading of planning CTs.

Table 5. Abdominal incidental findings

Finding	<i>n</i>	Percent of all abdominal findings	Clinical relevance (Lumbreras <i>et al</i> ⁷)
Adrenal nodule	5	2.39	Major
Focal hepatic hypodensity	1	0.48	Major
Gallstone	5	2.39	Moderate
Splenic artery aneurysm	3	1.43	Moderate
Dilated renal calices	1	0.48	Moderate
Axial hiatal hernia	79	37.80	Minor
Cystic hepatic lesion	66	31.58	Minor
Hepatic steatosis	20	9.57	Minor
Hepatic calcification	8	3.83	Minor
Splenic calcification	6	2.87	Minor
Renal cyst	4	1.91	Minor
Splenic cyst	3	1.43	Minor
Renal calcification	2	0.96	Minor
Cutaneous fibroma	2	0.96	Minor
Pneumobilia	1	0.48	Minor
Focal hepatic hyperdensity	1	0.48	Minor
Nephrolithiasis	1	0.48	Minor
Pancreatic cyst	1	0.48	Minor
Total	209	100	

All findings in our study, retrospectively diagnosed by two independent readers, were previously unknown. In particular, even with knowledge on planning CT results, re-evaluation of chest radiographs was unable to detect clinical findings, thereby questioning the diagnostic value of initial chest radiographs in the context of breast cancer.

We advocate thorough reading of planning CTs for radiotherapy, to fully exploit the diagnostic potential of this modality.

Notably, even in diagnostic chest CT scans, up to 63.2% of thoracic incidental findings remain unreported by the radiologist.^{20,21} Attention regarding incidental findings is needed among the radiologist community.

Study strengths

Compared with the literature, our study is the most exhaustive on a study cohort of 382 patients. Furthermore, we limited inclusion to patients with non-metastatic breast cancer to ensure a homogeneous study population. Moreover, independent reading by two experienced radiologists ensured validity of the data. Finally, our study is the first to systematically categorize clinical incidental findings according to their clinical relevance.

Study limitations

Our study is mainly limited by its retrospective design. Furthermore, only breast cancer patients were included, thereby limiting generalizability to other tumour entities. Moreover, the study is limited by the information given in the tertiary hospital electronic patient records. For example, incidental findings might have been diagnosed previously but were unreported in the electronic record. However, this pragmatic scenario resembles the clinical routine in most healthcare systems without centralized electronic patient record. Finally, the scan range with incomplete coverage of the abdomen might have biased results on abdominal findings.

CONCLUSION

Planning CTs are an integral component of radiotherapy for breast cancer patients. Routinely, reading is performed by radiation oncologists.

However, considering the relevant number of additional clinical findings, additional reading by experienced radiologists might be yielded. These clinical findings might significantly influence clinical management and outcome.

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