

CT Appearances of Post-Radiation Livers in Patients with Unresectable Cholangiocarcinoma

Piyaporn Apisarnthanarak MD*, Krongkan Kanchanarat MD*,
Kobkun Muangsomboon MD*, Walailak Chaiyasoot MD*,
Nantakan Ieumwananonthachai MD**, Pittayapoom Pattaranutaporn MD**

* Division of Diagnostic Radiology, Department of Radiology, Faculty of Medicine Siriraj Hospital,
Mahidol University, Bangkok, Thailand

** Division of Radiation Oncology, Department of Radiology, Faculty of Medicine Siriraj Hospital,
Mahidol University, Bangkok, Thailand

Objective: To characterize the computed tomographic (CT) findings of post-radiation livers and the interval changes in patients with unresectable cholangiocarcinoma.

Material and Method: Thirteen patients with unresectable cholangiocarcinoma who received concurrent chemoradiation with conformal radiotherapy technique (50 to 66 Gy, 2 Gy/fraction) were included in the present study. CT at pre-radiation and sequential follow-up at 1, 3, 6, 9 and 12 months were retrospectively reviewed by two abdominal radiologists to identify CT characteristics of post-radiation liver and the interval changes.

Results: CT at pre-radiation and sequential follow-up at 1, 3, 6, 9 and 12 months were available in 92.3%, 100%, 76.9%, 53.8%, 30.8% and 23.1%, respectively. Post-radiation livers showed sharply-delineated, hypodense radiation areas, which were well related with the isodose line of 35 to 56 Gy (mean = 44.4 ± 6.55 Gy). These radiation areas were mostly appreciated on portal venous phase at 1-month follow-up study in 12 of 13 (92.3%) patients and these were gradually less defined in subsequent studies. Progressive decrease size of radiation areas with persistent enhancement on delayed phase images were recognized. Progression of hepatic cortical irregularity was seen in four (30.8%) patients, as well as pulmonary fibrosis of lung bases.

Conclusion: Post-radiation liver in patients with unresectable cholangiocarcinoma showed a sharply-defined, hypodense radiation area, which was mostly appreciated in 1-month follow-up CT and was gradually less defined in subsequent studies with evidence of progressive atrophic change.

Keywords: Computed tomography CT, Conformal radiotherapy, Radiation-induced liver disease RILD

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Conventionally, hepatic irradiation has a limited role for the treatment of hepatic malignancies because of the concern about radiation effect to normal liver, so called radiation-induced liver disease (RILD)⁽¹⁾. It is characterized by hepatomegaly, ascites and elevated liver enzymes (esp. alkaline phosphatase), usually found when the hepatic radiation dose is more than 35 Gy⁽²⁾. Nevertheless, there are new radiation techniques (*i.e.* intensity-modulated radiotherapy (IMRT) and conformal radiotherapy (CRT)), which focus the radiation beam around tumor area and

reduce the radiation dose to nearby healthy liver. With these advanced techniques, radiation has emerged as an alternative treatment to unresectable, primary and secondary hepatic malignancies⁽³⁻⁷⁾, at the same time as decreasing the prevalence of RILD. Few prior studies⁽⁸⁻¹³⁾ have described the computed tomography (CT) findings of post-radiation liver seen in patients with and without clinical signs of RILD. Of these, most were case reports and had no serial follow-up studies. Willemart et al⁽⁹⁾ described a sharply-delineated region of hypodense radiation area on portal venous phase that showed persistent enhancement on delayed phase in one patient, explained by accumulation of contrast due to veno-occlusive change after hepatic radiation. Unger et al⁽¹⁰⁾ reported the same pattern of post-radiation change in another patient. For systematic review of CT findings of post-radiation

Correspondence to:

Apisarnthanarak P, Division of Diagnostic Radiology,
Department of Radiology, Faculty of Medicine Siriraj Hospital,
Mahidol University, Bangkok 10700, Thailand.
Phone: 08-1924-0038, Fax: 0-2412-7785
E-mail: punpae@yahoo.com

livers and the interval changes, the authors designed this retrospective cohort study in patients who were enrolled in the prospective clinical trial using concurrent chemoradiation treatment for unresectable cholangiocarcinoma. They were scheduled to have sequential follow-up CT studies at 1, 3, 6, 9, and 12 months after complete radiation.

Material and Method

Patients

The present study was a single-centered study conducted at Siriraj Hospital, a 3,000-bed university hospital in central Thailand. The present study was approved by the hospital institutional review board. Written informed consent was waived due to the retrospective design. Between January 2005 and April 2008, all patients who were enrolled in the prospective clinical trial using concurrent chemoradiation treatment with CRT for unresectable cholangiocarcinoma and had available follow-up CT studies were included in the present study. All of them had the biopsy proven of primary hepatic adenocarcinoma.

Concurrent chemoradiation

All participants in the present study received intravenous Gemcitabine with a dose of 300 mg/m² weekly for a maximum of 6 cycles and CRT with a total dose of 50-66 Gy (mean 59.4 Gy); 2 Gy/fraction. The treatment planning was performed by a CadPlan@ and Eclipse version 8@, Varian Medical Systems, Finland. The treatment machine was a Varian C2300 with multileaf (120 leaves) collimator, Varian Medical Systems, Finland.

CT studies

Due to the retrospective design, the participants' CT studies were performed by various CT scanners, including in-house CT scanners [a spiral CT scanner (AV1, Philips, Netherlands) and two multislice (16- and 64-slice) CT scanners (both were LightSpeed, GE Healthcare, United Kingdom)] with a variety of outside CT scanners. Hence, there was a variety of CT techniques, including slice collimation (1.25 mm-10 mm) and dynamic post-contrast sequences.

The participants' CT studies at pre-radiation and sequential follow-up at 1, 3, 6, 9 and 12 months after complete radiation were retrospectively reviewed by two abdominal radiologists who were blinded to the participants' radiation details (e.g. radiation

fields, received doses) and laboratory findings. Any discrepancies in their opinions were solved by a consensus review by both radiologists.

Image analyses

First, each radiologist separately identified a hepatic hypodense area in the earliest available follow-up study and termed it as a radiation area (RA). Then, the RA was retrospectively compared with the CT planning for CRT to identify the isodose radiation line that was closely matched with the figure of RA. The same RA was identified in pre-radiation study and subsequent follow-up studies. The rest of the liver was labeled as a non-radiation area (NA). Then the following data was obtained:

1) The outline of the RA: Each radiologist categorized the RA in each follow-up study as "a sharply-delineated area" or "a poorly-delineated area".

2) The difference in attenuation between the NA and the RA (NA-RA) on pre-contrast and dynamic post-contrast images: For each CT study, the attenuation of the RA and the NA were measured in Hounsfield unit (HU), by selecting a representative region of interest (ROI) as large as possible (ranging from 200 to 400 mm²) and avoiding areas of visible tumor, hepatic vessels and biliary structures. The same locations were measured on pre-contrast and dynamic post-contrast images. Then, the difference in attenuation between the NA and the RA was calculated (NA-RA) for each CT sequence.

3) Size of the RA: First, the authors identified the greatest diameter (cm) of the RA on the earliest follow-up study of each participant. Then, the same diameter was identified and measured on each follow-up study and was subsequently compared with pre-radiation study. The difference in the greatest diameter of the RA between pre-radiation and each post-radiation study was calculated (PRE-POST). In case of unavailable pre-radiation study, the first follow-up study was used as a baseline to compare with subsequent studies.

4) Post-radiation hepatic cortical irregularity: The hepatic cortex of the RA on the first available study was categorized as "smooth" or "irregular". Then, hepatic cortex of the RA on each follow-up study was compared with the most recent, available study (i.e. 1-month follow-up study compared with pre-radiation study, 3-months follow-up study compared with 1-month follow-up study) and was categorized as "increased hepatic cortical irregularity", "unchanged",

or “decreased hepatic cortical irregularity”. In case of “increased hepatic cortical irregularity” with other possible causes (*e.g.* tumor involvement), it was recorded as “unchanged”.

5) Post-radiation biliary system abnormality: The biliary system on the first available study was categorized as “normal” or “abnormal” (*i.e.* irregularity, dilatation). Then, the biliary system on each follow-up study was evaluated by comparing with the most recent, available study and was categorized as “increased biliary system abnormality”, “unchanged”, or “decreased biliary system abnormality”. In case of “increased biliary system abnormality” with other possible causes (*e.g.* tumor invasion), it was recorded as “unchanged”.

6) Post-radiation vascular abnormality: The hepatic vessels (portal vein and hepatic veins) on the first available study were categorized as “normal” or “abnormal” (*i.e.* irregularity, thrombosis). Then, the hepatic vessels on each follow-up study were assessed by comparing with the most recent, available study; and were categorized as “increased vascular abnormality”, “unchanged” or “decreased vascular abnormality”. In case of “increased vascular abnormality” with other possible causes (*e.g.* tumor invasion), it was recorded as “unchanged”.

7) Post-radiation pulmonary fibrosis: Pulmonary fibrosis at lung base near radiation field was assessed on the first available study and was recorded as “pulmonary fibrosis” or “no pulmonary fibrosis”. Then, the degree of pulmonary fibrosis on each follow-up study was compared with the most recent, available study and was categorized as “increased pulmonary fibrosis”, “unchanged” or “decreased pulmonary fibrosis”. In case of “increased pulmonary fibrosis” with other possible causes (*e.g.* infection), it was recorded as “unchanged”.

Statistical analyses

Descriptive analysis was employed to assess participants’ demographic data, the availability of CT studies at each time frame and the seven CT characteristics of post-radiation changes. To test the difference in attenuation between NA and RA (NA-RA) on each CT sequences and the difference in the greatest diameter of RA between pre-radiation and each follow-up study (PRE-POST), Wilcoxon’s signed ranks test was applied. The p-value less than 0.05 was used for statistically significant difference. All statistical data analyses were performed by using SPSS version 19.0.

Results

Patients

During January 2005 to April 2008, 16 consecutive patients with unresectable cholangiocarcinoma underwent concurrent chemoradiation with CRT at the authors’ institution. Two of these were lost from the follow-up program soon after complete radiation. One patient did not have available follow-up CT study for re-evaluation. The remaining 13 patients contributed as the present study population. These included 11 males and 2 females, with the age range between 35-67 years (mean = 55.5, SD = 10.29). None of the participants developed RILD after radiation.

CT studies

CT at pre-radiation and sequential follow-up at 1, 3, 6, 9 and 12 months were available in 12 patients (92.3%), 13 patients (100%), 10 patients (76.9%), seven patients (53.8%), four patients (30.8%) and three patients (23.1%), respectively.

The available 49 CT studies included 47 (95.9%) in-house and two (4.1%) outside studies. For the two outside studies, only thick slice images (5-10 mm) were obtained. For 47 in-house studies, the images were ranging from thick-sliced images (5-10 mm) from conventional CT scanner (10 studies, 20.4%) to thin-sliced images (1.25-1.5 mm) from multidetector CT scanners (37 studies, 75.5%). For total 49 studies, 39 studies were complete with pre-contrast and triple post-contrast phases (including arterial, portal venous and 5-minutes delayed phases), but 10 studies were incomplete (4 studies had only portal venous phase, 3 studies had pre-contrast and portal venous phases, and 3 studies had pre-contrast, arterial and portal venous phases).

Image analyses

1) The outline of the RA: At 1-month follow-up, 12 of 13 (92.3%) studies showed sharply-delineated, hypodense RA, which were mostly appreciated on portal venous phase. Another patient developed a sharply-delineated hypodense RA at 3-months follow-up study; also was mostly appreciated on portal venous phase. These hypodense RA were well related with the isodose line, ranging from 35 to 56 Gy (mean = 44.4 ± 6.55 Gy). These areas were gradually less defined in subsequent studies, starting from three months after radiation (Fig. 1). In one patient (7.7%), the RA persisted as a sharply defined area until nine months after radiation (Fig. 2). Unfortunately, the mean resolution time could

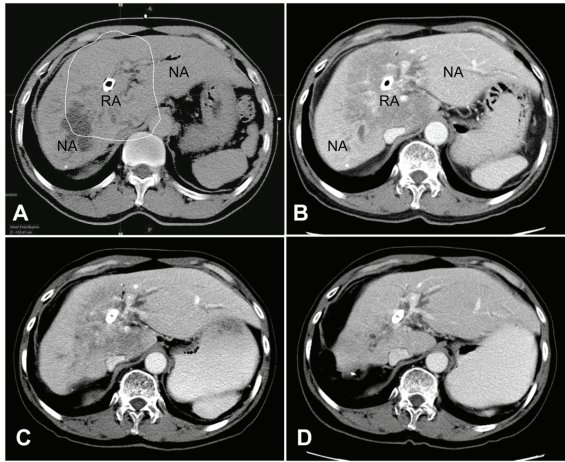


Fig. 1 67-year-old man with post-radiation change in liver
 A) Axial pre-contrast CT planning for CRT showed an isodose line of 45 Gy (white line) dividing a radiation area (RA) from a non-radiation area (NA)
 B) Axial CT on portal venous phase at 1 month after radiation showed a sharply-delineated, hypodense radiation area (RA) comparing to a non-radiation area (NA). The figure of RA was closely matched with an isodose line of 45 Gy (Fig. 1A)
 C) Axial CT on portal venous phase at 3 months after radiation showed atrophic change of a radiation area with gradually less-defined outline
 D) Axial CT on portal venous phase at 9 months after radiation showed progressive atrophic change of a radiation area with no delineated outline

not be calculated due to incomplete serial follow-up studies.

2) The difference in attenuation between the NA and the RA (NA-RA) on pre-contrast and dynamic post-contrast images: The median of the difference in attenuation between these two areas of each CT sequence is displayed along the time frame in Table 1. Interestingly, some of the median of the difference in density between these two areas were minus in value, esp. on 5-minutes delayed phase since 1-month after radiation. These represented that the RA had persistent enhancement and appeared as a hyperdense zone compared to the NA on 5-minutes delayed phase (Fig. 2 E-F).

3) Size of the RA: The median of the difference in the greatest diameter of RA between pre-radiation and each follow-up study (PRE-POST) gradually increased along the time frame (Table 2), representing progressive atrophic change of RA overtime.

4) Post-radiation hepatic cortical irregularity (Fig. 2): Four (30.8%) patients had progression of

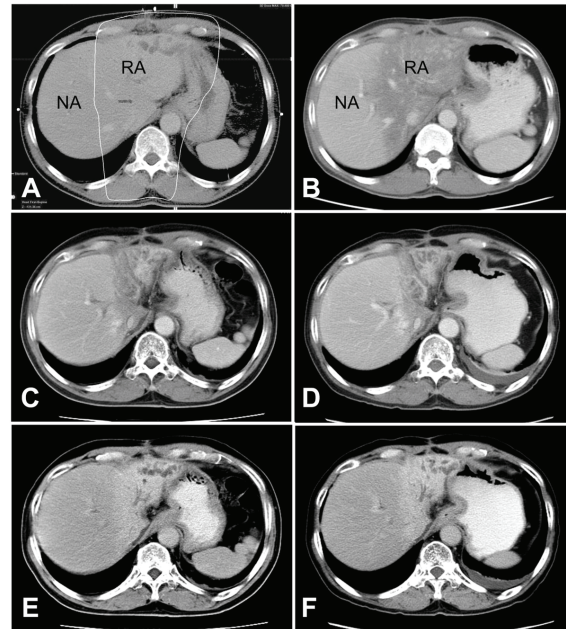


Fig. 2 55-year-old man with post-radiation change in liver
 A) Axial post-contrast CT planning for CRT showed an isodose line of 44 Gy (white line) dividing a radiation area (RA) from a non-radiation area (NA)
 B) Axial CT on portal venous phase at 1 month after radiation showed a sharply-delineated, hypodense radiation area (RA) comparing to a non-radiation area (NA). The figure of RA was closely matched with an isodose line of 44 Gy (Fig. 2A)
 C-D) Axial CT on portal venous phase at 6 months (C) and 9 months (D) after radiation showed progressive atrophic change of a radiation area with evidence of hepatic cortical irregularity. Notice that a radiation area persisted as a sharply-delineated, hypodense area until 9 months after radiation (D)
 E-F) Axial CT on 5-minutes delayed phase at 6 months (E) and 9 months (F) after radiation showed persistent enhancement of a radiation area, seen as a hyperdense zone compared to a non-radiation area

hepatic cortical irregularity of the RA after radiation (three at 3-months, and another one at 9-months follow-up studies).

5) Post-radiation biliary system abnormality: Improvement of biliary dilatation was identified in six and two patients at 1- and 3-months follow-up, respectively. These could be explained by regression of tumor size after radiation. Only two (15.4%) patients had progression of biliary dilatation (one at 6-months, and another one at 9-months follow-up), could be from

Table 1. The median (min, max) and p-value of the difference in attenuation (HU) between the NA and the RA (NA-RA) on pre-contrast and dynamic post-contrast studies displayed along the time frame

	Pre-radiation (n = 12***)	1-month (n = 13)	3-months (n = 10)	6-months (n = 7)	9-months (n = 4)	12-months (n = 3)
Pre-contrast						
Median (min,max)	1.0 (-3,10)	8.0 (-1,18)	8.5 (-19,37)	6.0 (-4,15)	6.0 (1,14)	9.0 (-5,19)
p-value	0.38	0.00	0.11	0.08	0.13	0.50
Arterial phase						
Median (min,max)	1.5 (-16,19)	6.0 (-10,34)	15.0 (-14,33)	0.0 (-9,18)	0.0 (-14,6)	3.0 (-9,15)
p-value	0.88	0.05	0.05	1.00	1.00	1.00
Portal venous phase						
Median (min,max)	-3.0 (-7,1)	25.0* (-2,41)	16.0 (-11,47)	-1.0 (-7,21)	-6.5 (-16,1)	7.0 (-14,12)
p-value	0.19	0.00	0.05	0.84	0.50	1.00
Delayed phase						
Median (min,max)	2.0 (-7,5)	-6.0** (-16,8)	-6.0** (-22,13)	-15.5** (-21,-10)	-15.0** (-31,3)	-9.0** (-16,-2)
p-value	1.00	0.02	0.12	0.03	0.25	0.50

* The maximum median of the difference in attenuation between these two areas was 25.0 HU on portal venous phase at 1-month follow-up study. This could explain why most radiation hypodense areas were mostly appreciated on portal venous phase at 1-month follow-up study and were less defined in subsequent studies

** The median of the difference in attenuation between these two areas on 5-minutes delayed phase were minus in value since 1-month after radiation, representing the persistent enhancement of RA on delayed phase images

*** The CT at pre-radiation was not available in 1 participant

Table 2. The median (min, max) and p-value of the difference in the greatest diameter of RA between pre-radiation* and each follow-up study (PRE-POST) displayed along the time frame

	1-month	3-months	6-months	9-months	12-months
Median (min,max)	0.95 (-0.2,2.2)	0.90 (0.5,4.3)	1.80 (1.0,8.0)	2.75 (2.1,4.7)	3.00 (2.4,4.8)
p-value	0.06	0.00	0.02	0.13	0.25

Notify the progressive atrophic change of RA overtime

* In case of unavailable pre-radiation study (n = 1), the 1-month follow-up study was used as a baseline to compare with subsequent studies

biliary stricture after radiation or a subtle progression of cholangiocarcinoma.

6) Post-radiation vascular abnormality: Two (15.4%) patients in the present study showed progressive vascular narrowing and irregularity (one at 1-month and another one at 3-months follow-up), could be from post-radiation changes or a subtle progression of cholangiocarcinoma.

7) Post-radiation pulmonary fibrosis: Four (30.8%) patients had progression of pulmonary fibrosis at lung bases near radiation field. Three participants developed pulmonary fibrosis after radiation (two at 1-month and one at 3-months follow-up). Another participant showed pulmonary fibrosis on pre-radiation study with progression of the disease

at 3-months follow-up study. The areas of post-radiation pulmonary fibrosis were well related with the isodose line, ranging from 15 to 48 Gy (mean = 33.3 ± 15.48 Gy) (Fig. 3). The participants who did not have pulmonary fibrosis received the radiation dose to the lung region, ranging from 25 to 60 Gy (mean = 38.4 ± 10.73 Gy).

Discussion

Radiation-induced liver disease (RILD) was reported as a reversible hepatic disease explained by radiation-induced veno-occlusive disease, followed by sinusoidal congestion, decreased portal venous flow, and subsequent fibrosis^(8,9). Clinically, the acute form of RILD has an onset at 2-6 weeks after radiation

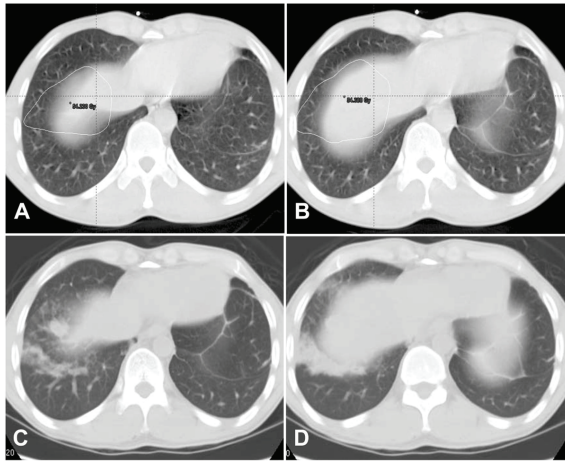


Fig. 3 37-year-old man with post-radiation pulmonary fibrosis
 A-B) Axial CT planning study for CRT (lung window display; A was superior to B) showed an isodose line of 48 Gy (white line)
 C-D) Axial CT images at 3 months after radiation (lung window display; C was superior to D) showed post-radiation pulmonary fibrosis at right lung base which was considerably matched with the contour of 48 Gy isodose line (Fig. 3A-B)

and most cases resolve within three months after radiation⁽¹⁴⁾. The present retrospective cohort study supported this explanation by revealing a sharply-delineated, hypodense RA which was mostly appreciated in the portal venous phase on 1-month follow-up study. This hypodense area was less defined in subsequent studies, representing its reversible nature. Yamasaki et al⁽¹¹⁾ reported that a sharp margin of hepatic radiation area was rarely seen. This could be explained by the CT follow-up time in their study was 8-12 weeks after radiation, when the sharp radiation margin was less defined.

In the same radiated area, it showed progressive smaller in size with persistent enhancement on 5-minutes delayed phase, which could possibly be explained by early veno-occlusive disease and subsequent fibrotic change after radiation as described in prior reports^(8,9). Unfortunately, some hepatic malignancies with large amount of fibrous component (e.g. cholangiocarcinoma and sclerosing hepatocellular carcinoma^(15,16)) may share the same enhancement pattern. Even the biliary obstructive pattern and the clinical of abnormal liver function can be found in both entities; and these may complicate the interpretation process. The information of prior radiation treatment and the sequential CT changes are

solely important clues to differentiate these two entities. Unfortunately, the present study had incomplete serial follow-up studies; hence, a comparison study between post-radiation changes and the progression of hepatic tumor could not be performed. Another study focused on this topic should be designed.

Interestingly, the hypodense RA in the present study related with a wide range of radiation isodose line (35-56 Gy, mean = 44.4 ± 6.55 Gy). Furthermore, a patient who had persisted, sharply-margined RA until nine months did not receive a higher radiation dose than the others (isodose line of 44 Gy). The authors assumed that each single liver had a different degree of radiation tolerance, depending on its own reserve, underlying degree of biliary obstruction and the received dose of chemotherapeutic agents. Nearby pulmonary fibrosis was also not well related with the received radiation dose, possibly explained by the similar reasons.

There were some recognized limitations of the present study. First, the sample size was small and focused on unresectable cholangiocarcinoma patients who primarily had initial biliary dilatation and elevated liver enzyme. They also received the addition of Gemcitabine. For these reasons, the present study population tended to have more severe hepatic injury from radiation and could not be the representative of the normal population. Second, unresectable cholangiocarcinoma patients had a short survival time. The median overall survival of the participants was 9.5 months (range 3-44 months) and 1-year overall survival was 37% (Ieumwananonthachai et al, presented at the 2009 annual meeting of the American Society of Clinical Oncology). Hence, the present study had incomplete serial follow-up studies. Furthermore, there were some missing data (e.g. the attenuation of the RA and the NA could not be obtained from outside CT studies) and variations of CT techniques (including slice collimation and dynamic post-contrast sequences). Third, the CT at pre-radiation was not available in one participant. In this case, the 1-month follow-up study was used as a baseline to compare with subsequent studies. Fourth, some CT findings such as the progression of biliary dilatation or vascular abnormality were rather subjective opinions and were not based on solid criteria. Although the authors tried to exclude other causes, the authors could not guarantee that these findings were solely from post-radiation changes, not from the progression of disease. Lastly, the authors used the largest diameter to represent the size of the RA

instead of the two diameters because it was easier for comparison. The accurate area and volume of the RA were too difficult to be calculated in part due to the irregularity of its contour.

In conclusion, post-radiation hepatic injury had CT characteristics as a sharply-defined, hypodense area, mostly appreciated on portal venous phase at 1-month follow-up study. It was gradually less visualized in subsequent studies, but could be appreciated until 9 months after radiation. Persistent enhancement on delayed phases and progressive atrophic change of radiated area could possibly be explained by early veno-occlusive disease and subsequent fibrotic change. The information of prior radiation treatment and the sequential CT changes are solely important clues to differentiate this condition from the progression of underlying hepatic tumors.

Potential conflicts of interest

None.

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ลักษณะการเปลี่ยนแปลงทางเอกซเรย์คอมพิวเตอร์ของตับหลังการรักษาโดยการฉายรังสีในผู้ป่วยมะเร็งทางเดินน้ำดีที่ไม่สามารถผ่าตัดได้

ปิยาภรณ์ อภิสารธนรักษ์, กรองกาญจน์ กาญจนรัตน์, กอบกุล เมืองสมบูรณ์, วลัยลักษณ์ ชัยสูตร, นันทกานต์ เอี่ยมวนานนทชัย, พิทยภูมิ ภัทรนุภาพร

วัตถุประสงค์: เพื่อศึกษาลักษณะการเปลี่ยนแปลงทางเอกซเรย์คอมพิวเตอร์ของตับหลังการรักษาโดยการฉายรังสีในผู้ป่วยมะเร็งทางเดินน้ำดีที่ไม่สามารถผ่าตัดได้

วัสดุและวิธีการ: ภาพเอกซเรย์คอมพิวเตอร์ก่อนและหลังการรักษาโดยการฉายรังสีด้วยวิธี conformal radiotherapy ที่ 1, 3, 6, 9, และ 12 เดือนของผู้ป่วยมะเร็งทางเดินน้ำดีที่ไม่สามารถผ่าตัดได้จำนวน 13 คน ได้รับการประเมินย้อนหลังโดยรังสีแพทย์ 2 คน เพื่อหาลักษณะการเปลี่ยนแปลงทางเอกซเรย์คอมพิวเตอร์ของตับหลังการรักษาโดยการฉายรังสี

ผลการศึกษา: ภาพเอกซเรย์คอมพิวเตอร์ก่อนและหลังการรักษาที่ 1, 3, 6, 9 และ 12 เดือน ที่มีให้ศึกษาคิดเป็นร้อยละ 92.3, 100, 76.9, 53.8, 30.8, และ 23.1 ตามลำดับ พบเนื้อตับบริเวณที่ได้รับการฉายรังสีมีลักษณะเป็น hypodense area ที่สัมพันธ์กับ isodose line ที่ 35-56 Gy (ค่าเฉลี่ย = 44.4 ± 6.55 Gy) ซึ่งเห็นขอบเขตได้ชัดเจนที่สุดใน portal venous phase ที่ 1 เดือนหลังการรักษา (ร้อยละ 92.3) โดยขอบเขตดังกล่าวจะค่อยๆ จางไปตามเวลา ร่วมกับมีการฝ่อเหี่ยวเพิ่มขึ้นของเนื้อตับบริเวณที่ได้รับรังสี นอกจากนี้พบขอบตับมีลักษณะขรุขระมากขึ้นร้อยละ 30.8 เช่นเดียวกับการมีพังผืดที่บริเวณชายปอดส่วนล่าง

สรุป: ลักษณะการเปลี่ยนแปลงทางเอกซเรย์คอมพิวเตอร์ของตับหลังการรักษาโดยการฉายรังสีในผู้ป่วยมะเร็งทางเดินน้ำดีที่ไม่สามารถผ่าตัดได้ พบ hypodense area ซึ่งจะมีขอบเขตชัดเจนที่สุด 1 เดือนหลังการรักษา และขอบเขตจะค่อยๆ จางไปตามเวลา ร่วมกับมีการฝ่อเหี่ยวเพิ่มขึ้นของเนื้อตับบริเวณที่ได้รับรังสี
