Stereotactic Body Radiation Therapy (SBRT) of Liver Tumors: Imaging Appearances and Implications on Evaluation of Response


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Disclosures

• None
Learning Objectives

• Describe SBRT induced changes in tumors and adjacent liver on CT, MRI and PET

• Describe limitations and possible interpretative errors in the evaluation of therapeutic response following SBRT

Target audience

• Radiologists, Radiology residents and fellows

• Radiation Oncologists
Stereotactic Body Radiation Therapy (SBRT)

• SBRT is a noninvasive method of treatment for primary hepatic tumors and selected patients with liver-confined metastatic disease.

• Ablative doses of radiation are delivered to a target volume in a single or small number of high dose fractions.

• SBRT is performed with steep dose gradient and rapid dose fall off outside of the target so as to minimize dose to adjacent normal tissues.

• Radiation to liver is minimized such that at least 50% of liver receives <19.2Gy.
Pathophysiology of SBRT in Liver

SBRT results in

- Coagulation necrosis (ablation) of target volume consisting of tumor and a safety margin of non tumor bearing liver (5-10mm)
- Inflammatory response in surrounding liver receiving non ablative radiation injury is histologically similar to veno-occlusive disease

Baseline CT showing tumor (yellow arrow), SBRT planning CT showing target volume. Follow-up CT showing hypodensity in tumor and reaction in adjacent liver included in the target.
Imaging changes after SBRT

- Tumors may show response, stay stable or progress following SBRT.
- Surrounding liver shows inflammatory response known as focal liver reaction (FLR) that is variable on duration following SBRT- a reflection of chronic changes that follow radiation and liver repair.
- Imaging after 3-6 months is most suitable for assessment.
- Currently there are no guidelines for follow-up and assessment of response in tumors undergoing SBRT.
Response to SBRT on CT

- Responding tumors show
  - reduced enhancement
  - reduced uptake on PET
  - gradual reduction in size over months
Response to SBRT on MRI

- Responding tumors show
  - reduced enhancement
  - reduced uptake on PET
  - gradual reduction in size over months
Response to SBRT on PET

• Responding tumors show
  • reduced enhancement
  • reduced uptake on PET
  • gradual reduction in size over months
Response to SBRT on CT

- Responding tumors show
  - reduced enhancement
  - reduced uptake on PET
  - gradual reduction in size over months

Baseline: 5.7cm
5 months: 4.5cm
9 months: 3.0cm
Response to SBRT on MRI

- Responding tumors show
  - reduced enhancement
  - reduced uptake on PET
  - gradual reduction in size over months

Baseline 5.1cm

3 months 3.3cm

6 months 2.8cm
Progression of disease

- Failure of response can be evidenced by increase in size of tumor or disease spread elsewhere

Baseline 3 months

3.9cm 7.9cm

Baseline 18m
Minimal change following SBRT

- Some tumors may show minimal change in enhancement and stay stable in size following SBRT suggestive of partial or no response.
Post SBRT changes in Liver-
Focal Liver Reaction

• SBRT also results in focal liver reaction (FLR) in normal or non-tumor bearing liver parenchyma around the tumor.

• The extent and degree of FLR is dependent on dose administered, SBRT technique, prior chemoembolization, concurrent chemotherapy and underlying chronic liver disease.

• The pathogenesis of FLR is not well understood but is similar to radiation induced liver disease (RILD) which manifests histologically as venoocclusive disease (VOD).
Pathophysiology of FLR

**Acute (1-3 months)**
- atrophy of the central hepatic cells
- severe sinusoidal congestion/hyperemia and hemorrhage
- mild dilatation of the central veins with red blood cells.

**Subacute (2-6 months)**
- fibrin deposition in central veins/sinusoids and activation of clotting mechanism
- Sub lobular veins show significant obstruction by fine collagen fibers.

**Chronic (>6 months)**
- Fibrosis of the central veins, collapse of some lobules and fibrous bridging
- Accumulation of Kupffer cells and in late stages loaded with hemosiderin.
- Liver parenchyma generally recovers and heals over months
- Lobular architecture may be distorted without any clinical manifestations.
Imaging appearance of FLR

**Acute (1-3 months)**

- Sinusoids in the irradiated area receive contrast agent later than normal in the portal venous phase leading to hypoenhancement.
- Enhancement similar to rest of the liver in the later phases as there is still clearing of contrast.
- No displacement of vessels through FLR differentiates from tumor.

Two examples of acute FLR. Hypodensity (black arrows) near target volume. Note the patent vessels through the FLR.
Imaging appearance of FLR

Subacute (2-6 months)

- Delayed or hypoenhancement on portal venous phase persists
- Hyperenhancement in the delayed phases due to reduced contrast clearing secondary to obstruction of central veins.

Baseline
Portal phase
Delayed phase
6 months
Arterial phase hyperenhancement is due to preserved arterial inflow into the FLR. This may be seen at any stage of follow up.

Also illustrated in this example is the delayed hyperenhancement that occurs in subacute phase.
Imaging appearance of FLR

Chronic (>6 months)

- FLR gradually returns to normal enhancement pattern but may remain hypoenhanced in portal venous phase and hyperenhanced in the late contrast phase.
- Some parenchymal atrophy especially if tumor is near the surface
- Decreased uptake of hepatocyte specific contrast reflects non-functioning hepatocytes or down regulation of transporter proteins
Uncommon findings in FLR

- Ring or rim like enhancement around treated tumor may be seen during early follow up likely representing a ring of FLR.

Ring or rim enhancement (black arrows is seen on arterial phase or early portal venous phase images and resolves during follow up)
Uncommon findings in FLR

- Ring or rim like enhancement around treated tumor may be seen during early follow up representing a ring of FLR. Seen especially on arterial phase or early portal venous phase.

Ring or rim enhancement (black arrows) is seen during early follow up MRI and resolves on further follow up. Note reduction in size.
Uncommon findings in FLR

- Signal loss (black arrows) in opposed phase may be rarely seen.

- Probably due to chronic hemorrhage and hemosiderin in Kupffer cells following venous congestion and extravasation of erythrocytes that are phagocytized by activated Kupffer cells.
Factors to Consider During Evaluation of Response

Hypodense FLR (black arrows) around tumor should not be interpreted as increase in size of treated lesion as reduction in size usually occurs after 3-6 months post SBRT.
Factors to Consider During Evaluation of Response

• Fiducial markers adjacent to tumors may result in streak artifacts that limits assessment.

On the CT performed after 7 months following SBRT, the target tumor was thought to be treated. However at 1 year, enlarging hypodensity seen suggesting progression of tumor. Note the fiducial marker (black arrow) next to tumor causing streak artifacts limiting assessment of size of the tumor.
Factors to Consider During Evaluation of Response

- MRI can be useful in assessing response if fiducial markers limit assessment on CT

Assessment of size of lesion difficult on CT performed after 6 months following SBRT. Reduction in size of tumor is well demonstrated on MRI consistent with response.
Factors to Consider During Evaluation of Response

- PET may also be useful in assessing response if fiducial markers limit assessment on CT.

Another example showing limitation of CT in assessing tumor size due to fiducial markers. Residual tumor seen on follow up PET scan.
Factors to Consider During Evaluation of Response

- Continuous thin rim enhancement should not be interpreted as residual tumor

Thin continuous rim of enhancement (black arrow) probably representing FLR/inflammatory response may be seen in late arterial or portal venous phase and should not be interpreted as residual tumor. The rim disappears on follow up confirming its benign nature.

Nodular rim or rim showing washout and/or similar to tumor before treatment should raise the suspicion of residual/recurrent tumor.
Summary

• SBRT produces ablative changes in tumor that typically results in reduced enhancement and gradual decrease in size over months.

• Focal liver reaction has variable appearance and may be dependent on dose administered and time interval since SBRT.

• Imaging features should be interpreted with consideration of changes induced by radiation in surrounding liver to avoid errors in response evaluation.

• MRI and/or PET may provide more information when CT features are difficult to interpret.
Take home points

• Earliest response in liver tumors to SBRT is reduction in enhancement.
• Reduction in size typically occur after 6-9 months
• Thin continuous enhancing rim around tumor is benign.
• Unusual appearances in surrounding liver should be interpreted with caution.
• MRI and/or PET may be useful for assessment of response when CT is uninterpretable.
References


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