Imaging findings after abdominal radiation therapy in oncologic patients.

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Learning objectives

- To describe radiological findings due to the effects of radiation therapy in the normal abdominal and pelvic organs.

- To differentiate these post-treatment changes from other diseases.
Background

Introduction:

Radiation therapy has been used for many years in the treatment of several abdominal and pelvic tumors as primary or adjuvant therapy.

The radiation is focused on the tumor but it affects not only the target organ but also damages surrounding tissues included in the radiation field.

In recent years, new radiation therapy methods have been designed to increase the amount of dose delivered in the target organ while reducing radiation dose over the neighboring normal tissues by the ability to more effectively focus and deliver radiation to the tumor. Nevertheless with some of these newer techniques the quantity of normal tissue exposed to low-dose radiation is greater, this is the case with three-dimensional conformal external-beam radiation. Other modern techniques like intensity-modulated radiation therapy (IMRT), stereotactic body radiation therapy (SBRT), brachytherapy, and radioembolization have also substantially decreased the damage to non-tumoral tissues.

Radiation procedure:

In our hospital most of the patients were treated with 3D Conformal Radiation Therapy, but we present also patients formerly treated with other techniques.

3DCRT is a volumetric image-based virtual simulation approach for defining tumor and critical volume in each patient. It started to be used about 20 years ago and it generally implies an increased number of radiation beams that are shaped to conform the dose to the target volume and shield normal tissues by using beam’s-eye-view system (BEV)

For this conformal therapy there is a need to accurately delineate the patient’s tumor and the organs at risk (critical normal tissues) and thus create an arrangement of beams that delivers the prescribed dose to the target volume while keeping the dose to critical normal tissues low enough to minimize the risk of complications. However there are an increased number of normal tissues receiving a low dose radiation.

Factors that have an influence in the response of different organs and tissues:
Sensitivity of different tissues to radiation depends on the turnover rate.

The response of the different organs to the radiation injury depends on the type of tissue, so the atrophy predominates in epithelial tissue and fibrosis with stromal tissue.

The risk of injury depends not only in the method of radiation delivery but also in the size, number and frequency of radiation fractions, volume of irradiated tissue and duration of treatment.

Other factors which also influence damage are the underlying pathologies such as diabetes mellitus and hypertension and also the preexisting organ function.

Concomitant chemotherapy can act synergistically to cause injury.

Also to keep in mind that new radiation techniques and other anticancer therapies have improved significantly the survival rates so post-therapeutic images have increased their complexity.
Findings and procedure details

We have reviewed and described different radiation effects in the abdominal and pelvic organs that can be detected on imaging techniques.

Liver:

The liver is often incidentally irradiated during radiation therapy for tumors in the upper abdomen (stomach, pancreas, gall bladder...), right lower lung, distal esophagus, right breast or thoracolumbar spine.

Radiation-induced liver disease is a clinical syndrome characterized by anicteric ascites and hepatomegaly.

The probability of the disease is based on the irradiated liver volume, the total dose, number of dose fractions and the duration of the treatment. Other predisposing factors are chronic diseases such as hypertension, diabetes mellitus, atherosclerosis, infections or prior surgery. The preexisting organ function also influences the risk, so patients with liver dysfunction (especially cirrhosis and fatty liver) are more prone to the post-radiation injury and they have a worse prognosis. Also, as in other organs, concomitant chemotherapy may add to the injury.

The dose tolerance of the whole liver is around 30-35 Gy, but a portion of liver with 3D radiation planning can be treated with doses as high as 70 Gy.

The threshold for the imaging changes is lower than for the clinical disease, thus most of the patients with radiation induced imaging findings are asymptomatic.

The disorder occurs as a result of a veno-oclusive disease, so the small branches of the hepatic and portal veins are damaged after radiation therapy. The liver is the only organ in which radiation histologic changes are more important on the veins than on the arteries.

There are two stages:

-Acute phase: In the first weeks (usually between 4 and 16 weeks after treatment),

there is a subtotal collagenous occlusion of small vein branches, hyperemia and diminished cellularity at microscopic level, which translates into increased water content and diminished perfusion.
The patients are normally asymptomatic but they may manifest the classic triad of hepatomegaly, ascites, and increased alkaline phosphatase. Sometimes there is upper right quadrant abdominal pain.

Imaging features are a sharply demarcated and nonanatomic area of parenchyma which is hypodense at CT, hypo or hyperechoic at US and, due to the increase of water, there is hypointensity at T1-weighted and hyperintensity at T2-weighted MR images. Fig. 1 on page 13

In the dynamic CT images the affected parenchyma shows hyperdensity in the arterial phase and hypodensity in the venous phase because of the increased arterial flow and decreased portal venous flow. In delayed phase may be a persistent enhancement due to the impaired outflow of blood.

In fatty liver, which is frequent in patients undergoing adjuvant chemotherapy, the characteristic pattern may be reversed, since the injured liver is more hyperdense than the rest of the parenchyma, due to reduced fatty infiltration. Fig. 2 on page 13

In this phase the treatment is supportive and in otherwise normal livers normally fully recover.

The imaging features evolve over time and 3-6 month after treatment the liver parenchyma shows hepatocellular regeneration and the radiological findings may improve or even completely resolve.

Fig. 3 on page 14 Fig. 4 on page 15

-Chronic phase:

Atrophy, fibrosis or both are seen over long term follow in some patients, affecting a demarcated region of the liver. Fig. 1 on page 13

Spleen:

The spleen is frequently irradiated for palliation in lymphoma and leukemia, also for treating splenomegaly and hypersplenism and it is also unintendedly radiated in the treatment of other abdominal tumors (stomach, pancreas…).

Lymphatic tissue is highly sensitive, however the splenic damage after radiation therapy is uncommon because the stroma is more resistant.

Lymphoid tissue can be destroyed within hours with doses as low as 4-8 Gy. Splenic fibrosis and atrophy may occur over 5-6 weeks after 35-40 Gy.
Imaging features after radiation are not specific, and they are usually similar to those of the liver. There is a well-defined but nonanatomic area of low attenuation on non-contrast and portal venous phase CT or low intensity on T1 weighted MR imaging.

A late manifestation of splenic irradiation can be seen as a small and shrunken spleen or atrophy of the treated area. Fig. 5 on page 16

Usually the effects are not clinically significant. Although total loss of splenic function may occur in patients who received a whole-spleen dose of more than 20 Gy and fulminant pneumococcal infections may follow.

**Pancreas:**

Pancreas is uncommonly injured in abdominal radiation therapy. Pancreatic acinar epithelium is more sensitive than islet cells.

Radiation causes necrosis and fibrosis, and the radiological appearance may mimic that seen in chronic pancreatitis. We can see atrophy, parenchymal calcifications and even irregularities in the pancreatic duct. Fig. 6 on page 17

**Kidneys:**

The kidneys are very sensitive; they are the dose-limiting organs for radiotherapy in the treatment of abdominal tumors because a dose of 28 Gy to both kidneys in 5 weeks or less frequently leads to renal failure. Kidney injuries tend to be permanent.

Loss of approximately 5% of the renal volume was found with an associated decline in renal function signaled by a 20% reduction in creatinine clearance.

The risk of renal failure increases with preexisting renal impairment (particularly if secondary to diabetes and hypertension) and with prior or concurrent chemotherapy.

**Acute radiation nephritis:** The kidney is still having a normal volume and shape; however glomerular damage is seen histologically.

**Chronic nephritis:** Months to years after treatment. Different radiological examinations demonstrate a poorly functioning and atrophic kidney but unobstructed and, as in other organs, we can identify geographic but nonanatomic areas of low attenuation or low T1 signal intensity. Fig. 7 on page 18

Renal parenchymal loss may be diffuse or focal. Fig. 8 on page 19 Compensatory hypertrophy of non irradiated kidney may occur.
Radiation-induced changes may mimic pyelonephritis, renal infarction, and, rarely, renal masses.

**Ureters:**

Ureters are very resistant because although the urotelium is very sensitive, they are composed predominantly by muscle, which is a quite resistant tissue.

Radiation-associated ureteral strictures are uncommon and late manifestations and they tend to be smoothly tapering. The strictures can cause hydroureter and hydronephrosis with a resultant impairment of renal function. They can be easily seen on delayed CT scans.

The strictures have to be differentiated from malignant ones which typically have an abrupt change in caliber and jagged margins.

**Urinary bladder:**

The bladder is the most radiosensitive organ of the urinary system because of the rapid proliferation of its epithelial cells. Radiation cystitis occurs in up to 12% of cases and is dose dependent.

**Acute phase:** The bladder wall becomes edematous and symmetrically thickened on CT and on MR images it is seen as high signal intensity in the outer layer of the bladder on T2-weighted and as increased mucosal enhancement on post-contrast T1-weighted images. Fig. 9 on page 20

**Chronic phase:** the bladder becomes small and it can not be fully distended due to fibrosis.

Hemorrhage and necrosis can occur, causing hematuria and clot formation which is normally easily differentiated from tumor.

A late and uncommon but life threatening complication of radiation cystitis is a bladder rupture.

**Gastrointestinal system:**
Gastrointestinal tube injury is an important cause of morbidity after radiation therapy. The small bowel, similarly to the kidneys, is often the dose-limiting organ for radiation therapy. Approximately half of patients who undergo pelvic radiation therapy will have some degree of permanent change in bowel habits that will affect their quality of life.

The different parts of gastrointestinal tract have diverse degrees of radiosensitivity. Small bowell is the most sensitive organ because of its rapid cellular turnover and the rectum is the least one, however rectum is frequently injured because of its fixed position and its proximity to other pelvic organs which are commonly irradiated.

**Stomach and duodenum:** Prepyloric and pyloric ulcers producing deformity, that could be similar to benign peptic ulceration, except that they may not heal.

There can lead to deformities, fixed narrowing and aperistaltic antropilolic region.

Radiology appearance on CT is nonspecific mural thickening, and sometimes perigastric fat stranding can be seen. Fig. 10 on page 21

**Small intestine:** despite being the most sensitive part of the gastrointestinal tract it usually receives fewer doses than the colon due to their high mobility, with the exception of terminal ileum which, due to its fixed position, is the most frequently affected area. Radiation injury is also called radiation enteritis and has two stages.

Acute phase: after few days or weeks of exposure. It is a mucosal process and there is edema, inflammation and mucosal sloughing. At CT, there is uniform wall thickening, with mucosal hyperenhancement. This phase is usually transient and self-limited and it will normally resolve. Predominant symptom is diarrhea. Fig. 11 on page 22 Fig. 12 on page 23

Chronic phase: It is a transmural process that can appear months to years after treatment. The overall incidence is 1%-5%. It is caused by submucosal obliterative vasculitis that results in ischemia, collagen deposition, and fibrosis. Fig. 13 on page 24 Some complications are fibrotic strictures that can cause bowell obstruction, impaired peristalsis and unusually complex fistulas (enteroenteric, enterocolic, or enterovesical) or bowell wall rupture.

Mesenteric fibrosis can also occur resulting in fixation of small bowel loops with tethering.

**Colon:** Radiation damage in colon is similar to the small bowell.

Radiological features are wall thickening, loss of distensibility with radiation strictures and narrowing.
The most affected part is rectum, and radiation induced proctitis is seen as a regular and symmetrical rectal wall thickening, with inflammation of the perirectal fat, increase in the presacral space, thickening of the perirectal fascia. Fig. 14 on page 25 Radiation induced colon cancer has been suggested.

Radiation induced changes have to be differentiated from neutropenic colitis (usually typhlitis) which affects cecum in immunosuppressed patients following chemotherapy. There is segmental bowel wall thickening with surrounding fat stranding and free fluid and patients are usually symptomatic.

**Uterus:**

In postmenopausal patients, radiation does not usually cause any changes, however the reduction of the tumor can cause alterations in uterine morphology, for example poor visualization of the cervix.

In premenopausal women, radiological features after treatment are the loss of distinction between junctional zone and outer myometrium, and the myometrium becomes linear and hypointense after 6 months,

Other complications are cervical stenosis after approximately 3-6 months. Uterine obstruction can lead to fluid accumulation and hydrometra, hematometra or pyometra may happen.

Fig. 15 on page 26

**Ovaries:**

Ovaries will decrease in size and signal intensity with loss of physiologic follicles after 6 months radiation treatment.

Ovarian function can be maintained in premenopausal patients by surgically repositioning them outside the radiation field.

**Male pelvic organs:**

After pelvic radiation in males prostate, seminal vesicles and testes may exhibit atrophy. The zonal anatomy of the prostate can be obscured on T2-weighted images.
Testes are unfrequently irradiated, and they will appear small and hyperechoic at ultrasound because of atrophy of stroma and fibrosis of glandular elements. It can result in hypogonadism and subfertility.

**Bone and muscle:**

The abdominal and pelvic bones are frequently affected by radiation (up to 90% of patients).

The first change seen is replacement of marrow bone by fat which occurs after 8 weeks.

Lately insufficiency fractures in the affected bone may occur and the most common places are the sacrum and pubic rami. Fig. 16 on page 27

Nonunion and aseptic necrosis are known complications.

Fractures are normally seen on follow up CT or MRI studies represented by a low signal fracture line in T1 on hyperintense bone marrow in T2 in typical locations. Fig. 17 on page 28 MRI can be more sensitive to detect these bone radiation changes and CT can better show the discontinuity in the cortical bone.

Radiation-induced tumors may appear and the most common in the abdomen and pelvis are bone and soft-tissue sarcomas, lymphoma, and mesothelioma. Most common imaging presentation is bone destruction with a soft tissue mass.

Myositis in striated muscle can occur, represented by high signal in T2-weighted images and increased enhancement in post-contrast T1 weighted images.

**Vascular injury:**

Vascular radiation injury in the acute phase involves the intima, whereas chronic changes affect the entire vessel wall.

There is often microvascular damage and small arteries and veins may be acutely occluded by endothelial proliferation and venous thrombosis resulting in impaired local perfusion. This may progress to endarteritis obliterans with ischemia and fibrosis of the supplied viscera.

Medium and large veins are rarely affected, but accelerated atherosclerosis and tissue damage with hyalinization and fibrosis can result.

Rarely, irradiated large vessels can rupture, this occurs mostly in carotid arteries and less frequently in aorta and femoral arteries.
**Fig. 1**: Patient treated with external beam radiation for gastric tumor a) Axial contrast-enhanced CT image shows normal shape and density of the liver in a CECT before treatment. (blue arrow) b) Post-treatment effects in the liver as a well demarcated and nonanatomic area of hypodense parenchyma area involving segments 3 and 4, related to acute radiation changes (yellow arrow), c) CT image at the same level, three years later showing focal atrophy of the involved segments due to chronic changes.

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Fig. 2: Patient who underwent external beam radiation therapy for a gastric carcinoma, in this case the liver was previously steatosic, so the attenuation pattern in the post treatment image is reversed: the irradiated parenchima is relatively hyperdense (blue arrow) related to the rest of the liver that shows still fatty infiltration.

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**Fig. 3:** Axial CT image of a woman who was treated with external radiotherapy for a right breast cancer. There is a non-anatomic area of low attenuation affecting the periphery of hepatic segment VIII, related to the radiation field.

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Fig. 4: a) Axial CT image with color overlays shows portal beams in the plan for 3D conformal external-beam radiation therapy in a patient with pancreatic cancer. b) Axial CT in the same patient after surgery and radiotherapy shows hypoattenuation (yellow arrow) and focal atrophy (red arrow) in the hepatic parenchyma affected by the beams.

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Fig. 5: a) CECT in a patient who underwent radiation for a gastric cancer, there is focal atrophy of the anterior pole of the spleen (red arrow). b) CT scan of the same patient acquired 5 years before radiation, showing a normally shaped spleen.

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**Fig. 6:** a) Axial CECT in a patient treated for a gastric carcinoma, we can see a moderate reduction of the volume of the pancreatic body and tail as compared to (b) CT image of same patient before treatment (4 years) showing a larger pancreas.

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**Fig. 7:** Axial CECT at the same level in a woman who underwent spinal irradiation for a vertebral metastasis in breast cancer. 

a) Normal kidneys before treatment. 

B) Non anatomic well demarcated area of low attenuation and cortical thinning in medial aspect of both kidneys (arrows). 

c) Evolution of focal atrophy of the kidneys in a later scan.

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Fig. 8: Axial (a) and coronal (b) CECT images of the abdomen presenting a focal area of atrophy involving the anterior area of upper third of the left kidney (red arrows) included in the field of radiation for a gastric tumor. c) CT scan of the same patient 5 years before with normal shape of that kidney (blue arrow).

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Fig. 9: Radiation cystitis. Patient who underwent pelvic radiation for a rectal carcinoma. a) Axial CECT and b) T2 weighted MR image showing a marked symmetrical wall thickening of the urinary bladder with increased mucosal enhancement due to radiation cystitis (arrows). c) On the DWI (b=600 s²/mm) the bladder wall shows a continuous band of high signal intensity.

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**Fig. 10**: a) Axial CECT in a patient who underwent external beam radiation for a gastric carcinoma, we can see mural thickening, mucosal hyperenhancement and perigastric fat stranding in the gastric antrum and the duodenal bulb. b) Image from the endoscopy showing post-radiation mucositis in the gastric antrum (biopsy also confirmed the diagnosis).

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**Fig. 11:** Axial (a, b) and coronal (c) CECT images show dilatation, important mural thickening with stratification and mucosal enhancement in jejunal and ileal loops in this patient who underwent pelvic radiation for ovarian cancer.

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Fig. 12: a) Axial CT with oral and iv contrast in a patient who underwent pelvic radiation for rectal carcinoma. Images show marked mural thickening of ileal loops and rectosigmoid colon and fat stranding related to radiation enteritis. (Ileostomy bag in the right lower quadrant). b) Axial CT with oral and iv contrast in the same patient before radiotherapy without bowel radiation changes.

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Fig. 13: Axial CECT (a) and abdominal ultrasounds (b) in a woman who was treated with radiotherapy for a uterine cervical carcinoma, more than 30 years ago. There is mural thickening of the ileal loops and sigmoid colon (blue arrows) and fat stranding. There are also extensive soft tissue calcifications (yellow arrow) affecting obturator muscles and pelvic fascias, secondary to an old scheme external radiation therapy for an advanced cervical cancer.

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**Fig. 14:** Chronic Radiation enteritis in a woman who underwent external beam radiation for a cervix carcinoma. CECT (a) and T2 weighted MRI (b) and (c) show mural thickening in rectal-sigmoid colon and small bowell (green arrows) with mesenteric fibrosis (orange arrow) related to chronic radiation enteritis.

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Fig. 15: Vesicovaginal fistula in a woman who was treated with external beam radiotherapy, surgery and brachiterapy for a cervical carcinoma. Conventional cystography (a) and sagittal plane reformatted image of CT urography in excretrory phase (b) where we can identify a comunication between the posterior wall of the urinary bladder and the vagina (yellow arrows) which is filled with the contrast coming from the bladder.

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Fig. 16: Axial (a) and coronal (b) CECT images of the pelvis show bilateral insufficiency fractures of the sacrum (arrows) in this woman who underwent pelvic radiation for a endometrial carcinoma.

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Fig. 17: a) Axial T1 weighted and b) sagittal T2 weighted MRI in a patient who underwent external beam radiotherapy and brachytherapy for a cervical carcinoma. There is replacement of bone marrow by fat due to radiation changes and we can see hypointense lines through both sacral wings and S2 related with insufficiency fractures. c) and d), same sequences than a) and b) show normal bone marrow before radiation therapy. Cervical cancer is also shown (white arrow).

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Conclusion

Although modern radiation techniques currently damage neighboring organs less than traditional therapy did, unintended exposure and damage does still occur. Also, many patients treated with older techniques have survived and they remain on follow up or have imaging studies for other reasons.

Radiation-related injury can be an important source of morbidity for patients and, sometimes, the imaging findings may resemble other pathologies and even tumor recurrence.

Evaluation of imaging studies in these patients requires an understanding of the expected post therapy changes to avoid misdiagnosis and to help establishing the correct treatment.