CANCER EDUCATION DAY

Post Radiotherapy Angiosarcoma

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Presenter Disclosure

- None

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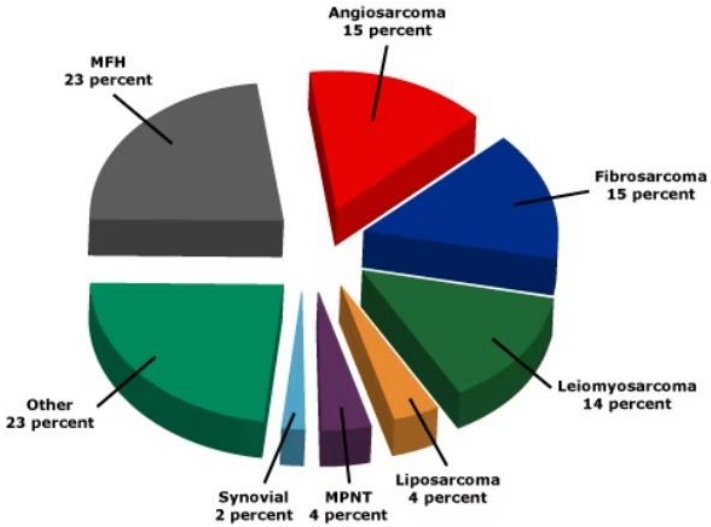
Epidemiology and risk factors

Low Incidence Rate

Radiation-associated sarcomas account for only 3-6% of all sarcomas.
Absolute risk is under 1% in exposed populations (0.09-0.14%).
Higher for breast sarcoma/angiosarcoma (0.4-0.8 %).

Common Primary Cancers

Most cases occur after breast cancer, lymphoma, head and neck, and gynecologic cancers.



Extended Latency Period

Risk persists 20-30 years after treatment.
Typical onset is 5-10 years post-radiation.

Risk Increases With Dose

Higher radiation doses correlate with increased risk, though can occur with doses below 40 Gy.
Others: age at radiation therapy and duration from primary treatment, exposure to chemotherapy.

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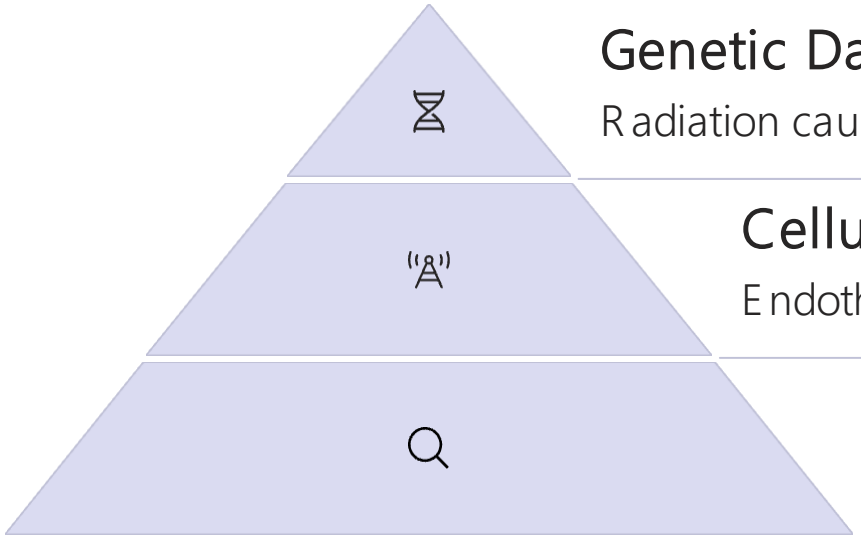
Am J Clin Oncol 1989; 12:411
Cancer 1991; 68:524
Int J Radiat Oncol Biol Phys 2019; 104:425

Pathophysiology



Genetic Damage

Radiation causes mutations in vascular endothelial cells

Cellular Transformation

Endothelial cells undergo malignant transformation

Vascular Proliferation

Abnormal blood vessel formation and growth

- Radiation must be sufficient to cause genetic damage but not cell death.
- MYC gene amplification is present in over 80% of radiation-induced angiosarcoma cases.
- High p53 signature

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J Clin Oncol 2023; 41:3735.
Int J Radiat Oncol Biol Phys 2013; 86:224

Clinical features

Skin Manifestations

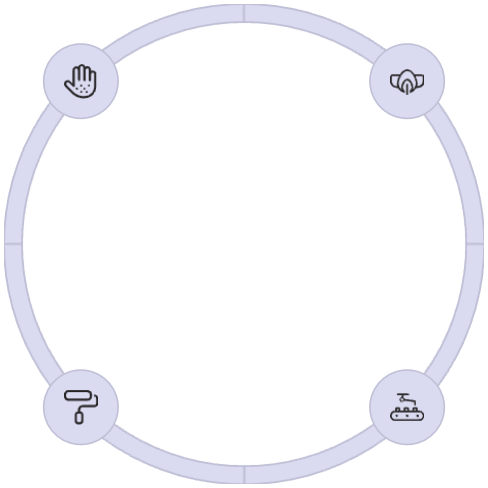
Ecchymotic macular or purplish papular lesions

- Often multiple lesions
- Can present with skin edema (peau d'orange)

Common Symptoms

Progressive, painless mass in radiation field

- Some report pain or compression symptoms
- Paresthesias or edema in extremities



Breast/Chest Wall

Common location after breast cancer treatment

- Primarily affects skin rather than parenchyma
- Often multifocal

Rectal/ gynecologic

Bleeding in rectal/gynecological

Cancer 1988; 62:2330.

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Radiologic diagnosis

MRI Imaging (Preferred)

Better delineation of soft tissue structures

Distinguish a radiation-associated sarcoma from a recurrence

CT Imaging

Useful for defining tumor size and local extent.

CT chest to detect pulmonary metastases

Mammography

May show trabecular thickening and skin changes separate from original breast cancer site.

Enhancing cutaneous nodules.

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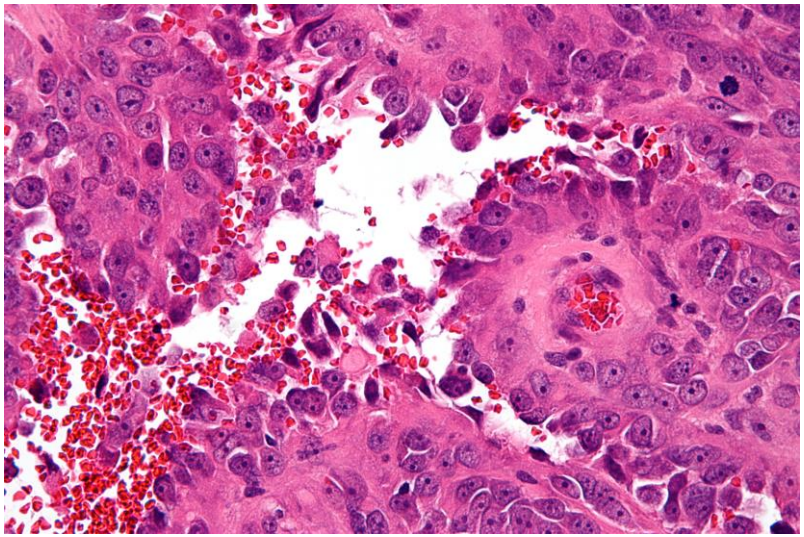
Pathology

Biopsy Planning

Multidisciplinary approach involving surgeon, radiologist, and pathologist. Complete staging studies before biopsy.

Histologic Examination

Shows irregular vascular channels lined by abnormal endothelial cells. Often high-grade with increased mitotic activity.



Immunohistochemistry

Positive for vascular markers: CD31 (gold standard), Factor-VIII, CD34, and VEGF.

Genetic Testing

MYC gene amplification present in majority of radiation-associated angiosarcomas. High p53 signatures.

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Cancer 1988; 62:2145
Carcinogenesis 2006; 27:1266
Mod Pathol 2012; 25:75

Prognosis

10-50%

5-Year Survival Rate
Lower than primary sarcomas

40-50%

Post-Resection Survival
When complete resection is achieved

50-65%

Local Recurrence Rate
Despite curative intent surgery

25-44%

Distant Recurrence Rate
Common sites: lung, liver, bone marrow

- Prognosis worse for angiosarcoma compared to other sarcomas, secondary angiosarcoma have worse prognosis compared to primary

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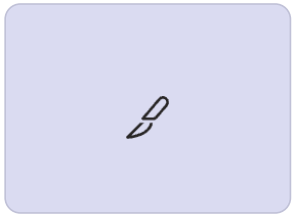
Eur J Cancer 2006; 42:2715.
Cancer 1980; 46:368.
Ann Surg Oncol 2012; 19:2700.

Management

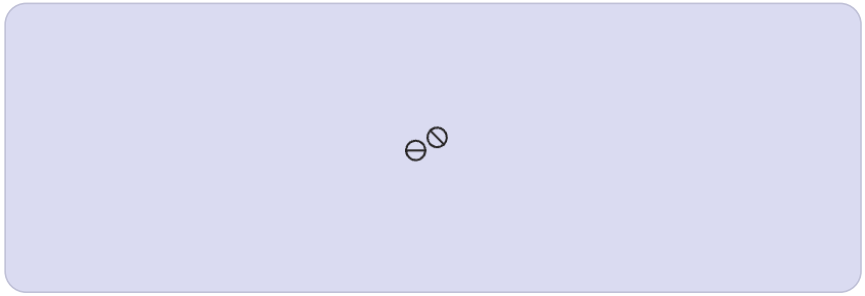


Surgical Resection

Mastectomy required for breast angiosarcomas

Reirradiation

Careful consideration in previously irradiated field



Systemic Therapy

Chemotherapy for high risk, metastatic or unresectable disease

Surgery

- Discussion in multidisciplinary team at a sarcoma center has shown improved outcomes
- High rate of local recurrence with breast conservative surgery
- 5 yr disease-specific survival for radical versus conservative resections was 86 and 46 percent, respectively
- Radical mastectomy with extensive resection and removal of previously irradiated skin with margin of 3 cm
- May requires a skin graft or myocutaneous flap.
- For clinically negative axilla, sentinel lymph node biopsy or axillary lymph node dissection is not routinely indicated

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Cancer 2003; 97:1832.
Breast Cancer Res Treat 2010; 122:619.

Radiation

Role of adjuvant RT is unclear

High rate of late effects of a high cumulative RT dose (rib fracture, pneumonitis, soft tissue necrosis)

High rate of disease recurrence with surgery alone (50 to 73 percent)

Reirradiation with a hyperfractionated schedule shown favorable results

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Breast 2010; 19:424.
Int J Radiat Oncol Biol Phys 2002; 52:620.

Chemotherapy

- Lack of prospective data, studies with mixed histology
- No clear benefit, ? disease-free survival/local control
- Individualized decision after thorough discussion
- Reasonable for tumour >3-5 cm, node positive, very close or positive margins
- Taxane preferred especially in patients who previously received prior anthracycline

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Ann Surg Oncol 2013; 20:1267.
Radiology 2000; 216:197.

Metastatic disease

- Treatment with palliative intent in most cases
- Patient with isolated pulmonary metastasis may be considered for metastasectomy
- Chemotherapy responses short lived,
- Taxane based chemotherapy most effective
- Others doxorubicin, liposomal doxorubicin, ifosfamide.
- Other therapies:
  - Tyrosine kinase inhibitors
  - Immunotherapy
  - Beta adrenergic blockers

BMC Cancer 2018; 18: 963
Cancer Manag Res 2018; 10: 1089-1114
J Immunother Cancer 2019; 7:213

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Conclusion

Post RT angiosarcoma is rare complication of breast radiation

Aggressive disease with tendency for local/distant recurrence and unusual sites of metastasis

Local disease treated with extensive surgery

Metastatic disease treated with palliative intent with chemotherapy, taxanes preferred

Br J Dermatol 2003; 148:606
J Immunother Cancer 2019; 7:213.

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Question & Answer