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MD Anderson Cancer Center
Making Cancer History®

Intratumoral Immunotherapies from an Interventional Radiology Perspective

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Disclosures

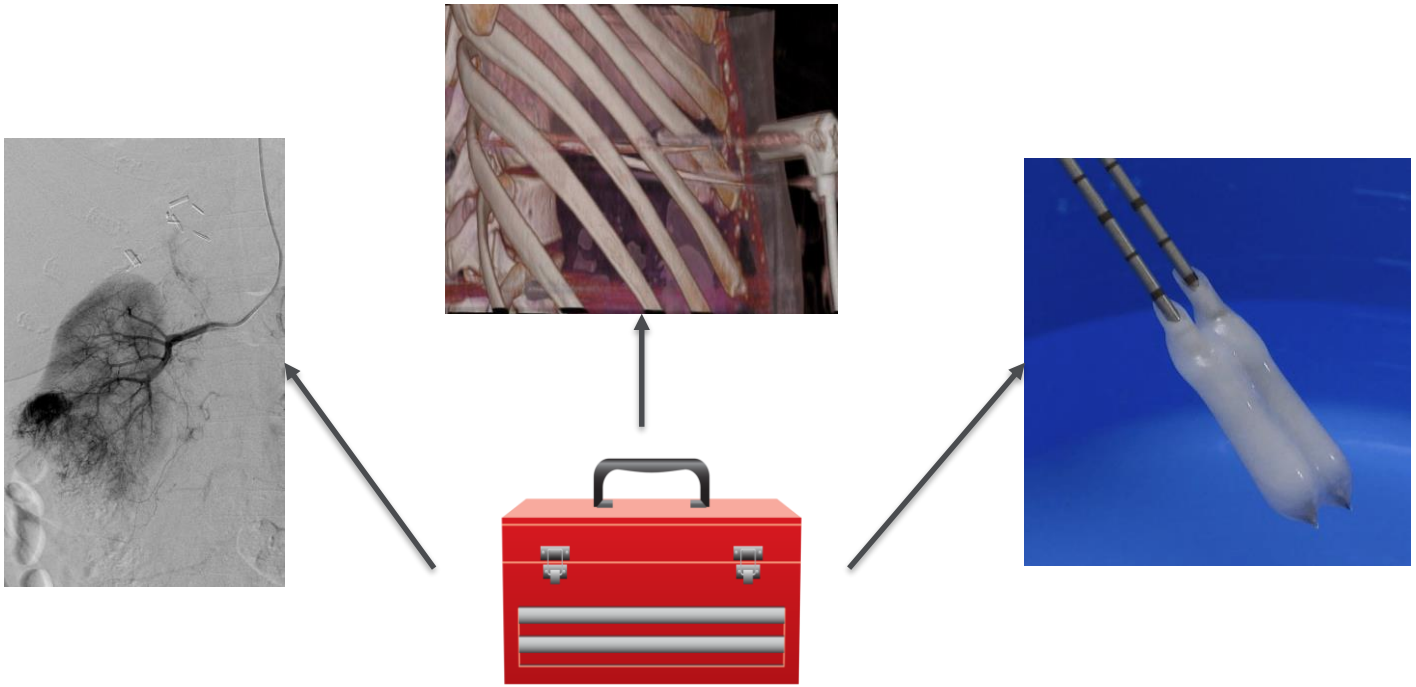
- None

Overview

- Interventional Radiology's contemporary immunomodulatory toolkit
- Image-guided delivery of intratumoral immunotherapies:
  - Is it safe?
  - What sites/organs can be targeted for injection?
  - What is the "best" lesion to choose for injections?
  - What is the "best" technique for injections?

Interventional Radiology

- Interventional Radiology has a long track record of delivering a diverse array of local tumor interventions that can have substantial immunomodulatory effects



Interventional Radiology

Trial #	Phase	Disease	Ablation modality	Immunomodulator	Endpoints
NCT02833233	Pilot	Breast cancer	Cryoablation	Anti-PD-1 antibody plus anti-CTLA-4 antibody	Safety
NCT02821754	I/II	HCC, biliary tract tumor	RF ablation or cryoablation	Anti-PD-1 antibody, anti-CTLA-4 antibody	Safety, PFS
NCT02626230	Pilot	RCC	Cryoablation	Anti-CTLA-4 antibody	Safety, RR
NCT02559024	I	Colorectal cancer	RF ablation	Anti-OX40 antibody	Safety, immune response
NCT02469701	II	NSCLC	Cryoablation	Anti-PD-1 antibody	RR
NCT02437071	II	Colorectal cancer	RF ablation	Anti-PD-1 antibody	Safety, RR
NCT02423928	I	Prostate cancer	Cryoablation	DCs, cyclophosphamide, anti-CTLA-4 antibody	Safety
NCT02311582	I/II	Malignant glioma	Laser ablation	Anti-PD-1 antibody	Safety, PFS, OS
NCT02250014	I	Prostate cancer	Cryoablation	GM-CSF	Immune response, PSA level
NCT01853618	I	HCC, biliary tract tumor	RF ablation or cryoablation	Anti-CTLA-4 antibody	Safety, feasibility, RR, TTP, OS

Intratumoral Immunotherapy

- A tremendous amount of creativity and energy has been applied to developing immunotherapeutics to modulate local tumor immune microenvironments
- Interventional Radiology's role is to ensure the safe and effective delivery of these therapies to the intended targets
  - At MD Anderson, we have performed over 800 encounters in Interventional Radiology for patients receiving intratumoral immunotherapy (both standard of care and investigational)

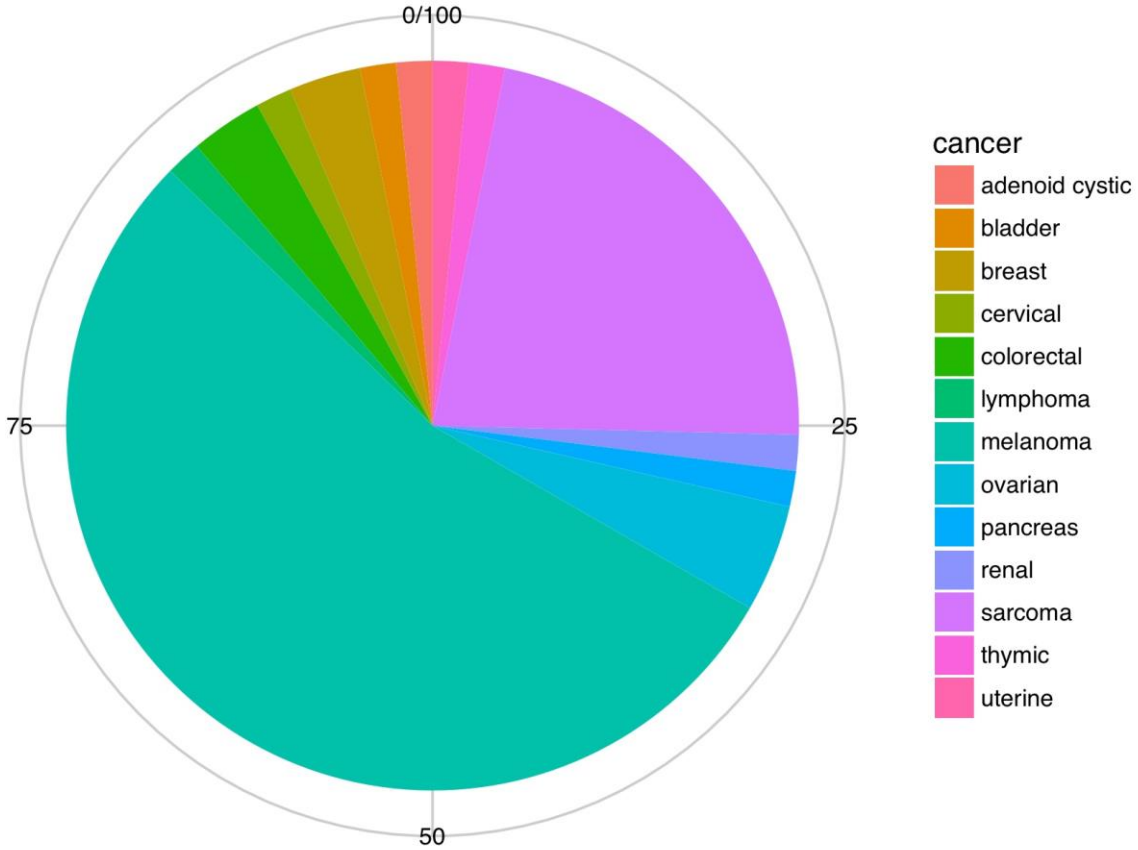
Intratumoral Immunotherapy

Take home point #1:

- These trials are complex! Median encounter/patient = 6
- Many moving parts (pharmacy, research nursing, blood draws, procedure schedules)
- Involve Interventional Radiology early

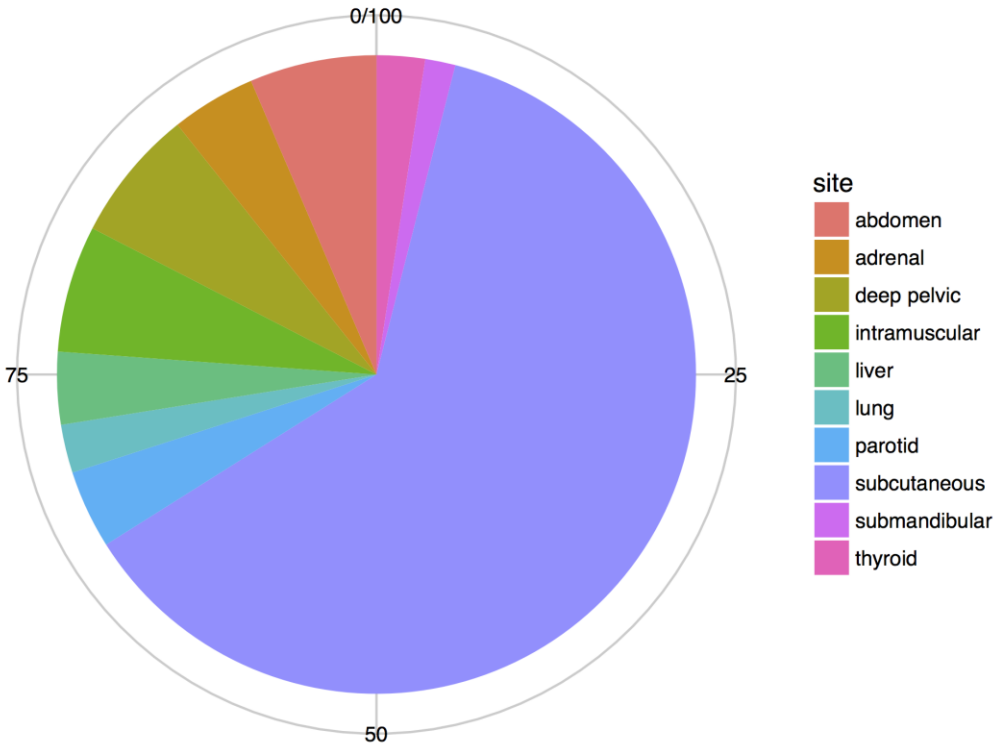
Sheth RA *et al.* SITC 2018

Intratumoral Immunotherapy



Sheth RA *et al.* SITC 2018

Intratumoral Immunotherapy

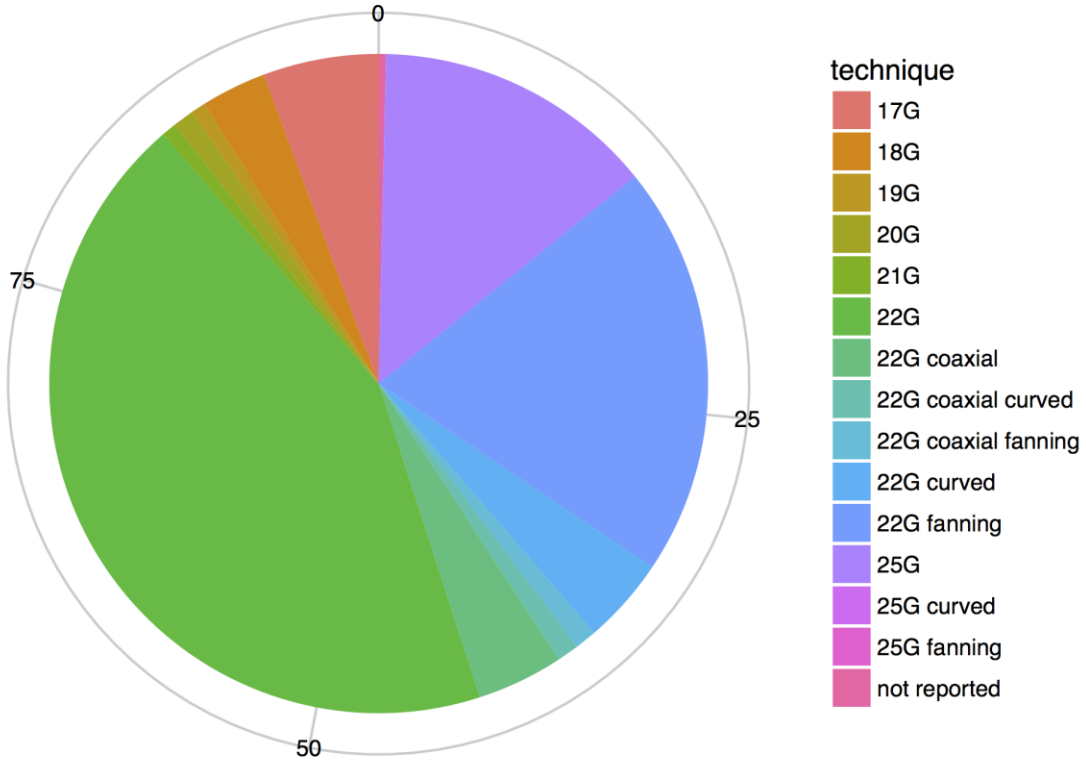


Take home point #2:

- i.t. delivery can be performed in deep, visceral lesions

Sheth RA *et al.* SITC 2018

Intratumoral Immunotherapy



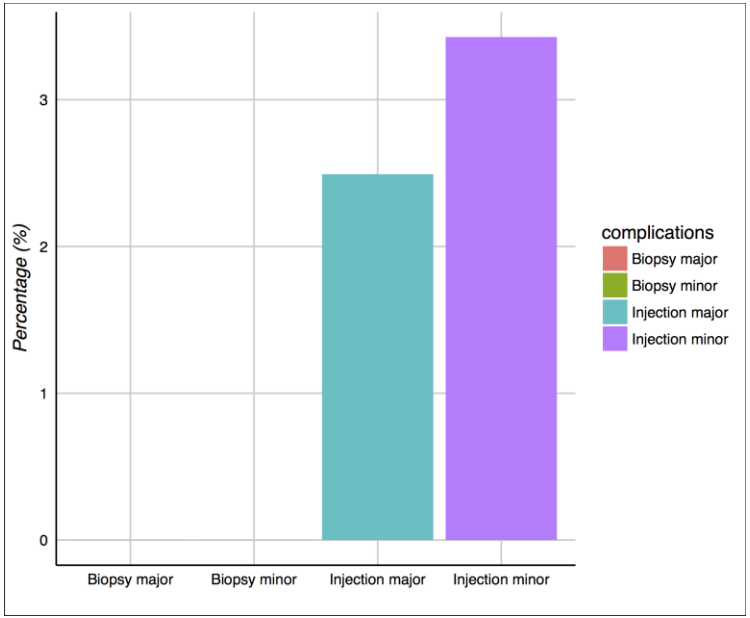
Take home point #3:

- There is no standardized technique for i.t. delivery

Sheth RA *et al.* SITC 2018

Intratumoral Immunotherapy

Injection-related complications within 24 hours

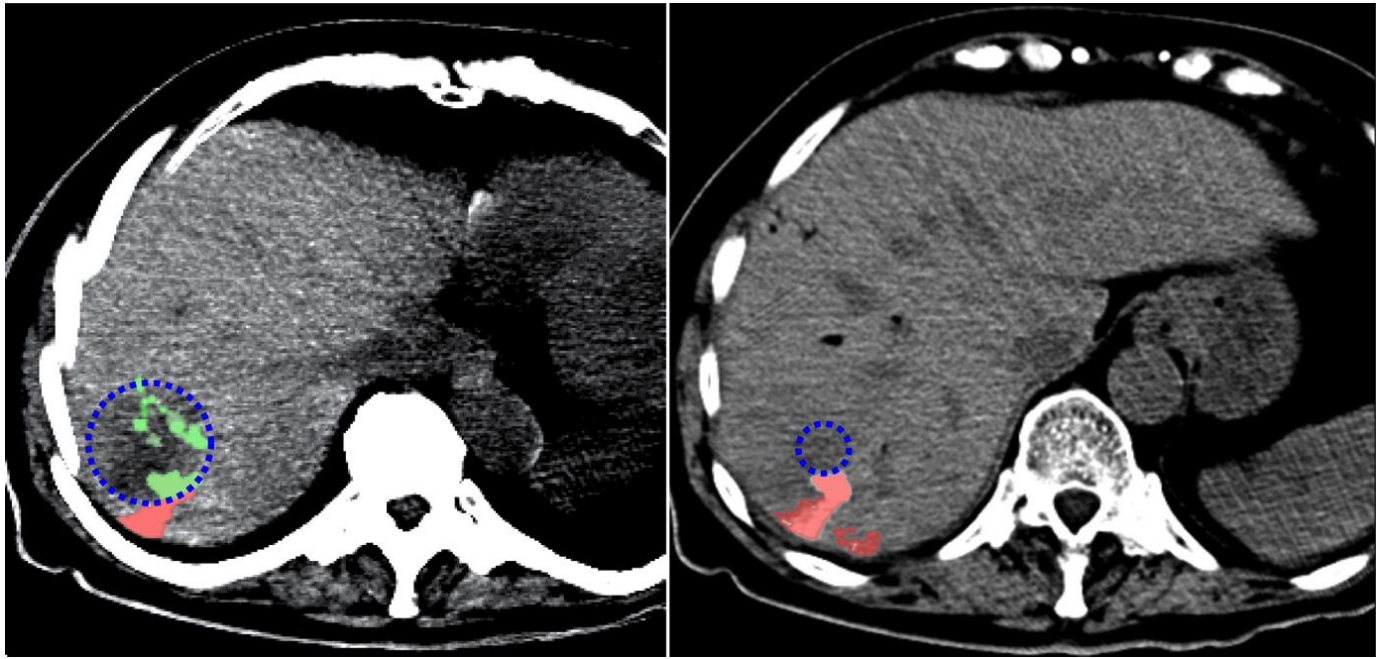


Take home point #4:

- Treatment teams need to be familiar with complication profile, especially those who are not used to treating immune-related adverse events

Sheth RA *et al.* SITC 2018

Optimizing i.t. drug delivery

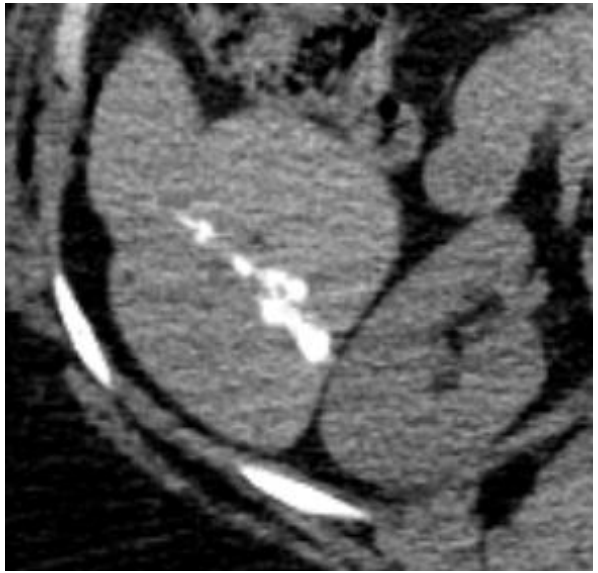


Optimizing i.t. drug delivery

The good...

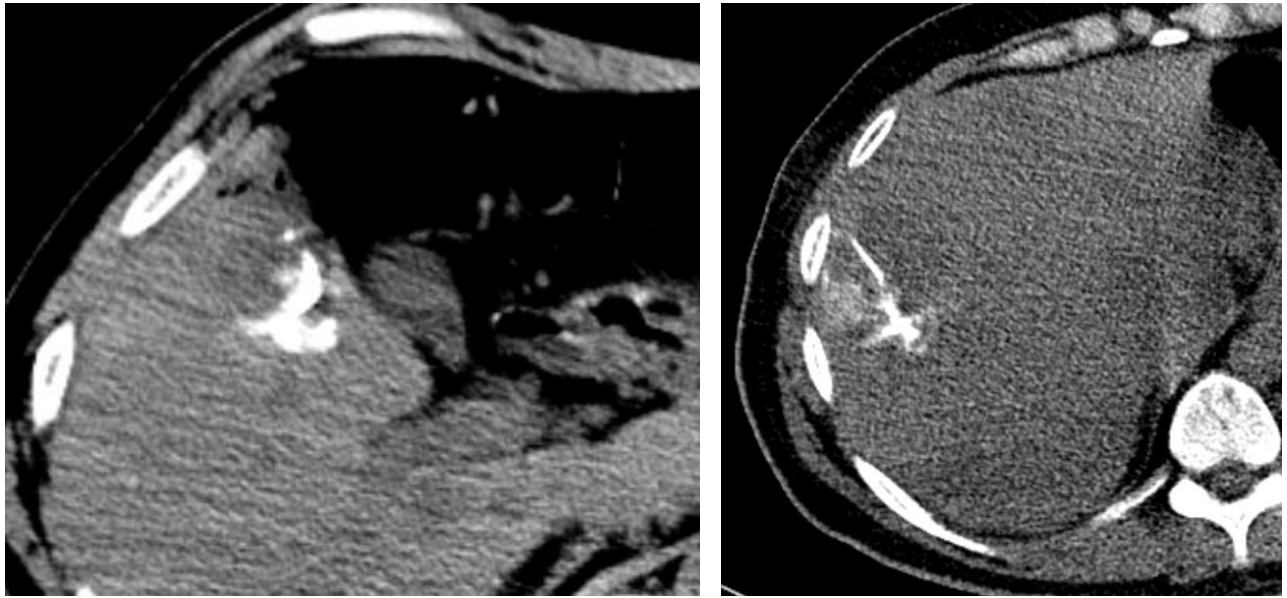
Optimizing i.t. drug delivery

The bad...



Optimizing i.t. drug delivery

The ugly...

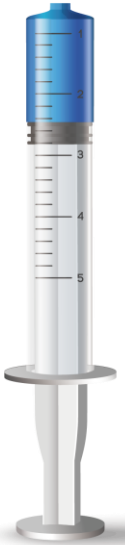


Optimizing Intratumoral Injections

Injection technique

+

Drug



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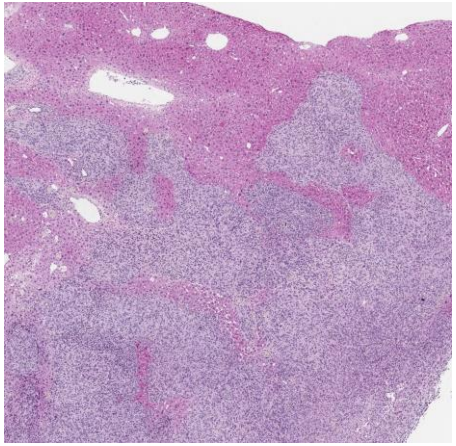
Tumor stroma

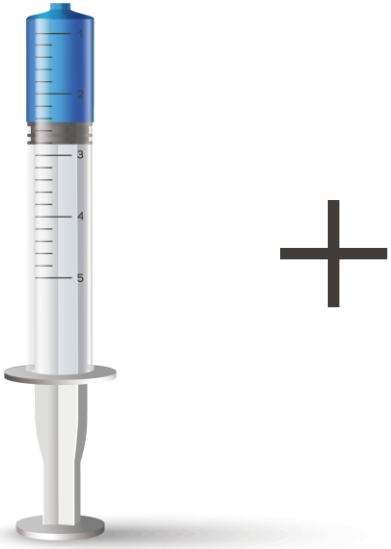


Optimizing Intratumoral Injections

Injection technique

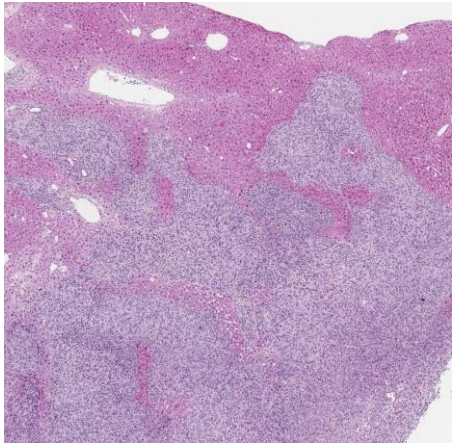
Needle design, injection technique

Drug



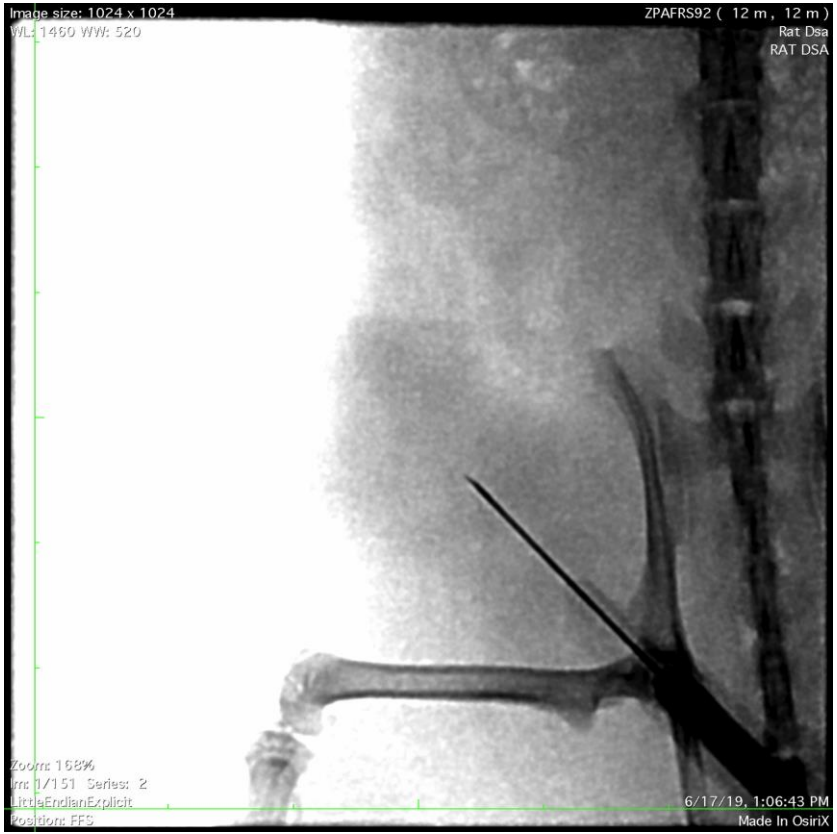
Viscosity, chemistry, controlled release technology

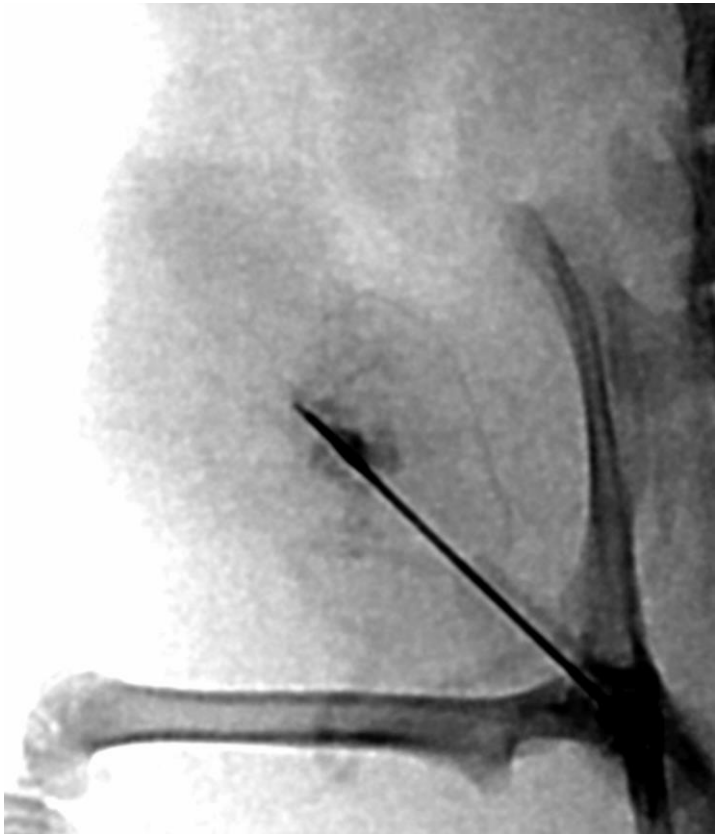
Tumor stroma



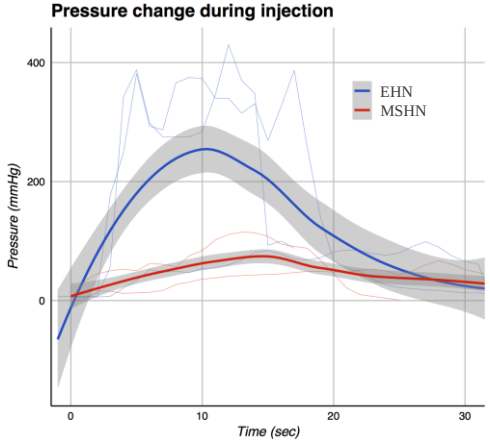
Radiation? Ablation? Enzymatic degradation?

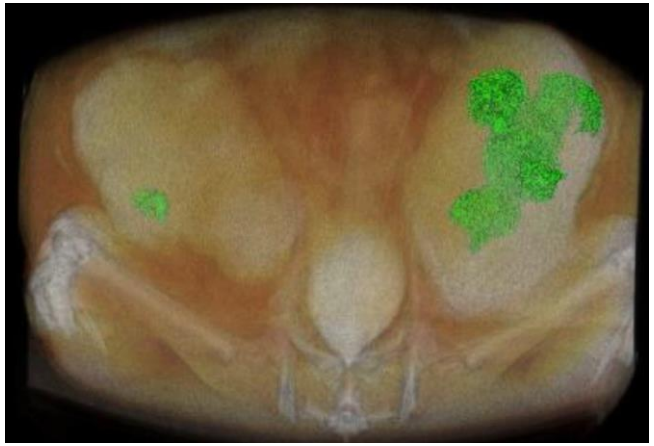
Optimizing Intratumoral Injections

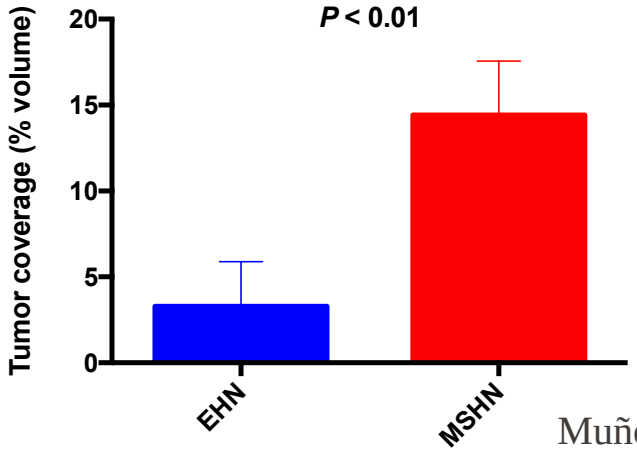




Optimizing Intratumoral Injections

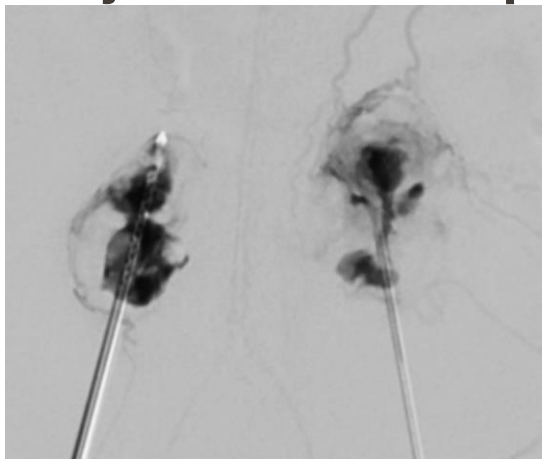






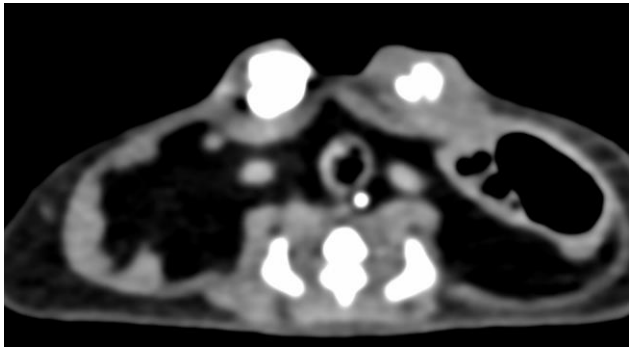
Muñoz *et al*. ASCO-SITC 2019

Injection technique

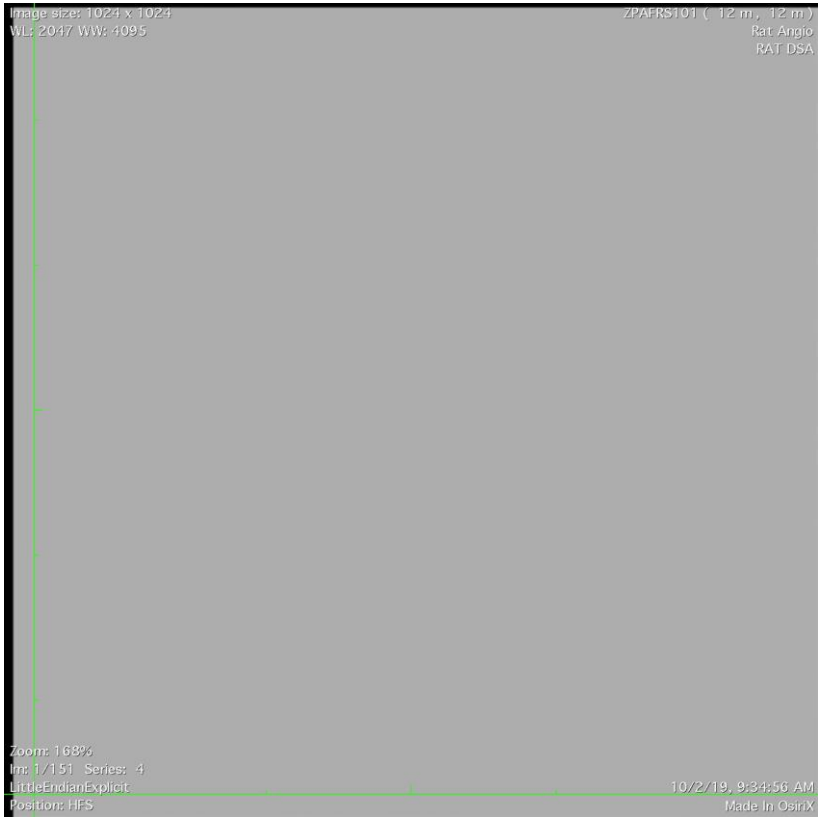


Intra-procedural

5 minute post

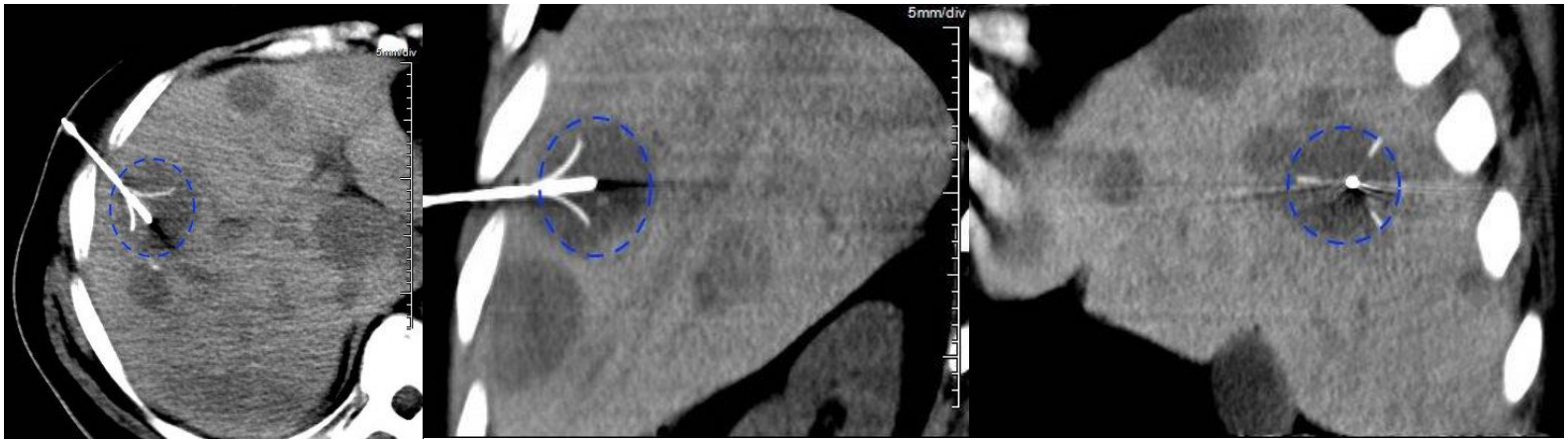


7 minute post

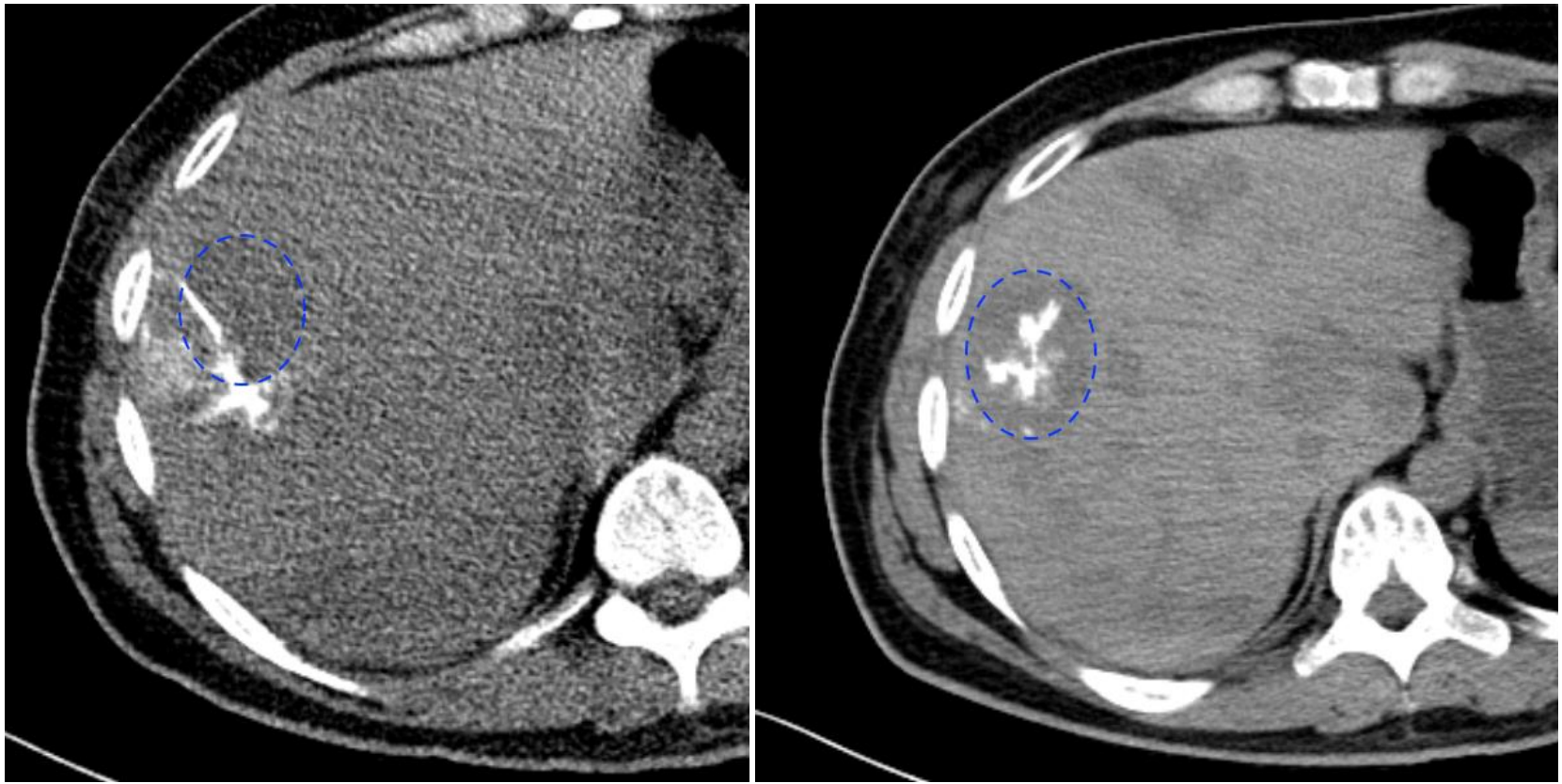


Injection Technique

Injection Technique

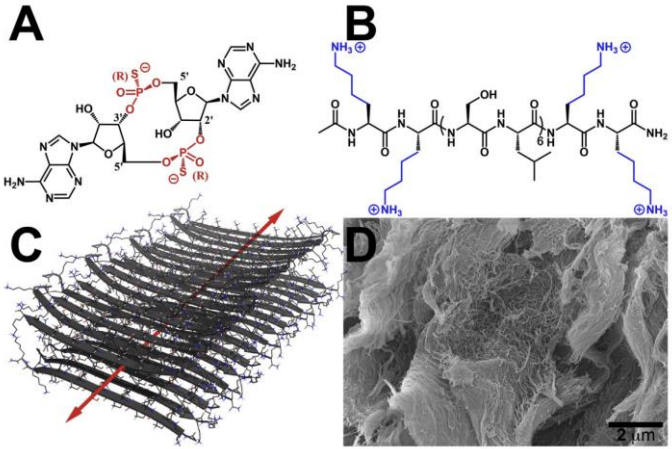


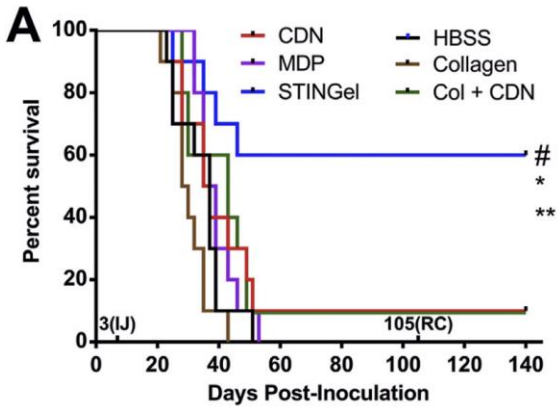
Injection Technique

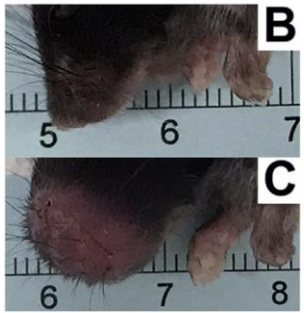


Optimizing Intratumoral Injections

Drug





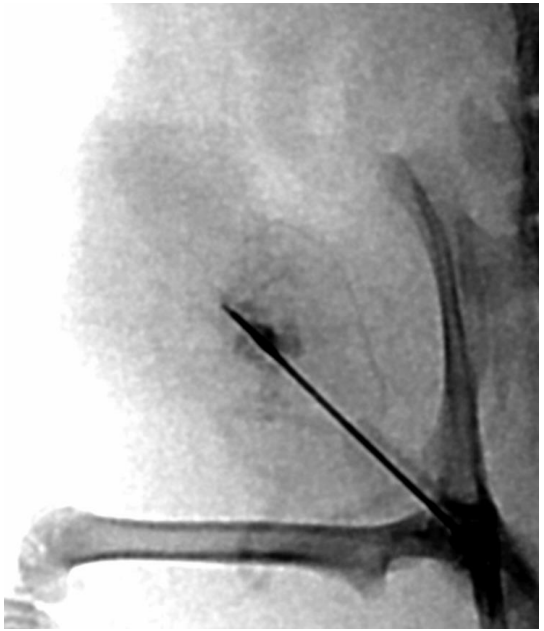


STINGel: Controlled release of a cyclic dinucleotide for enhanced cancer immunotherapy

David G. Leach [a, 1], Neeraja Dharmaraj [b, 1], Stacey L. Piotrowski [b], Tania L. Lopez-Silva [a], Yu L. Lei [c], Andrew G. Sikora [d], Simon Young [b, **], Jeffrey D. Hartgerink [a, *]

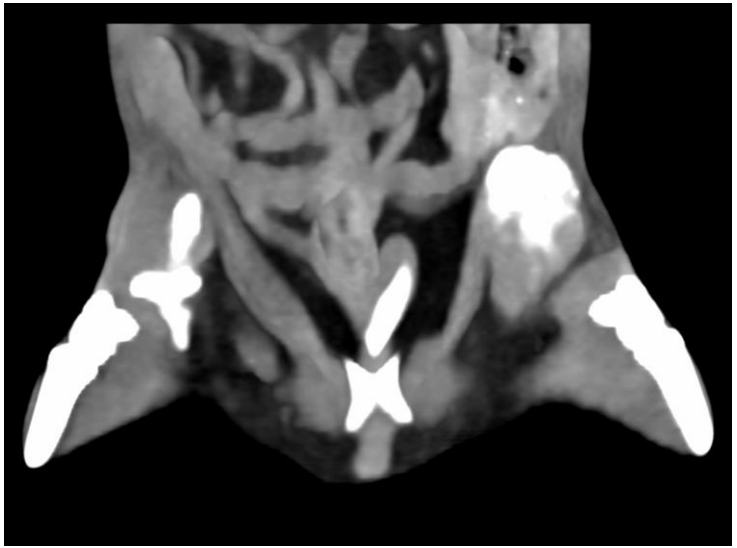
Optimizing Intratumoral Injections

Drug



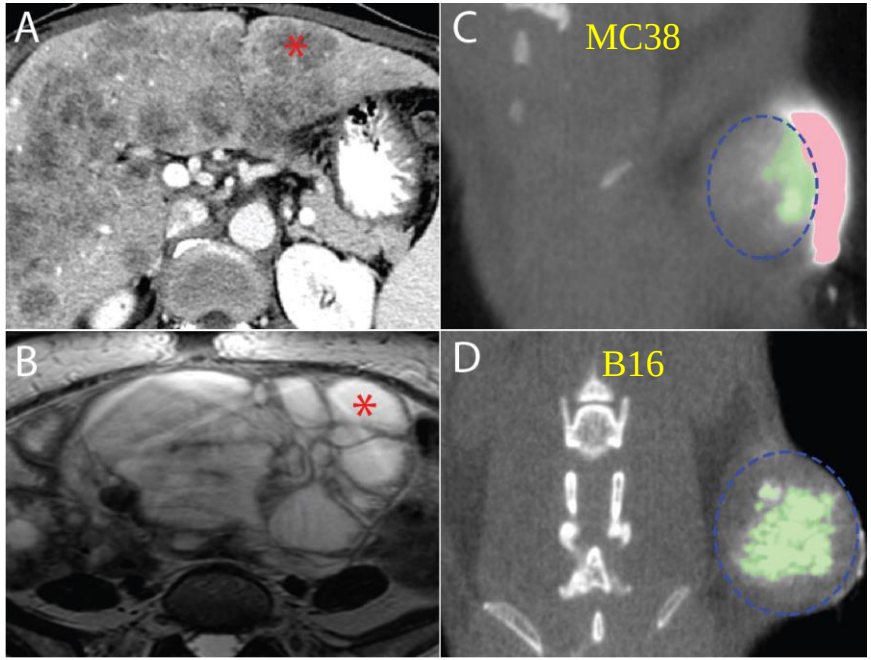
Free iohexol

MDP + iohexol



Optimizing Intratumoral Injections

Tumor stroma



How do we turn ”hard” tumors “soft”?

The need for standardization

- There is an immediate need for standardization of i.t. delivery techniques
  - To allow for meaningful comparisons across therapies
  - To minimize variations between operators and institutions
  - To optimize efficacy and minimize toxicities of the therapies

Summary

- Intratumoral immunotherapy trials are complex. Involve your Interventional Radiology colleagues early.
- Intratumoral immunotherapies can be delivered to subcutaneous as well as deep, visceral lesions.
- Interventionalists and their clinical teams need to be familiar with acute immune-related adverse events
- Delivery techniques need improved standardization and evidence-based practices
- Tremendous opportunity for innovative applications of bioengineering, nanomedicine, image analysis, etc.
  - The creativity in techniques to optimize i.t. delivery can match the creativity in developing the therapies themselves!

Thank you!

Collaborators

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Crystal Dupuis

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