Multicompartment Lymphatic Failure

Christopher L. Smith MD PhD

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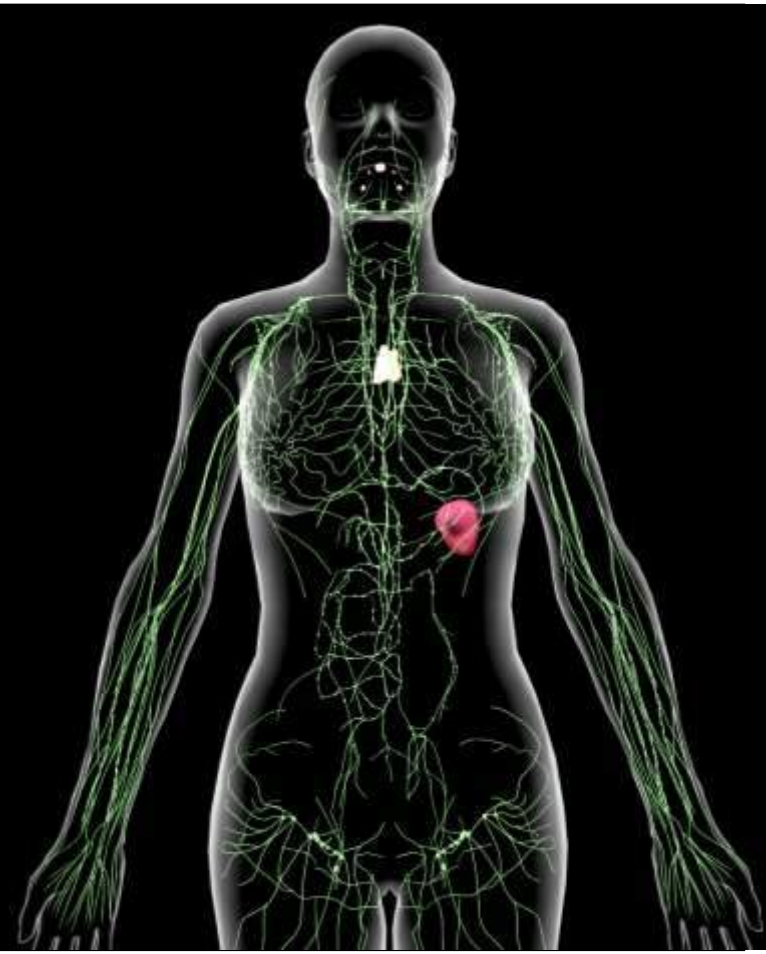
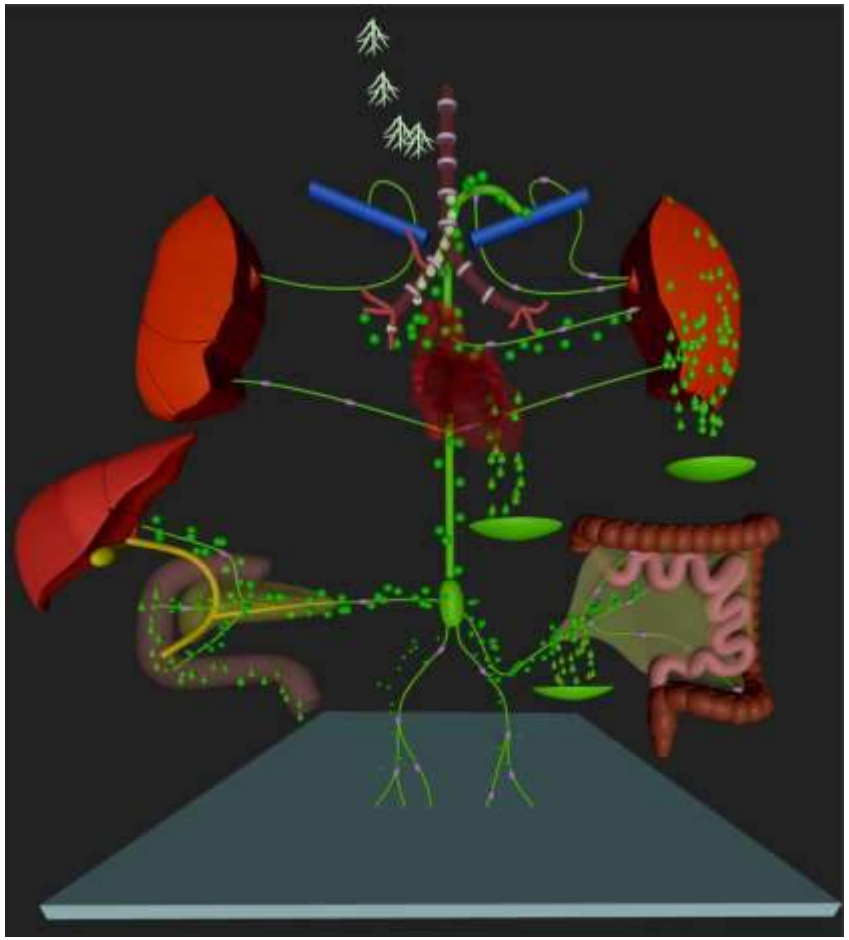
Children's Hospital of Philadelphia

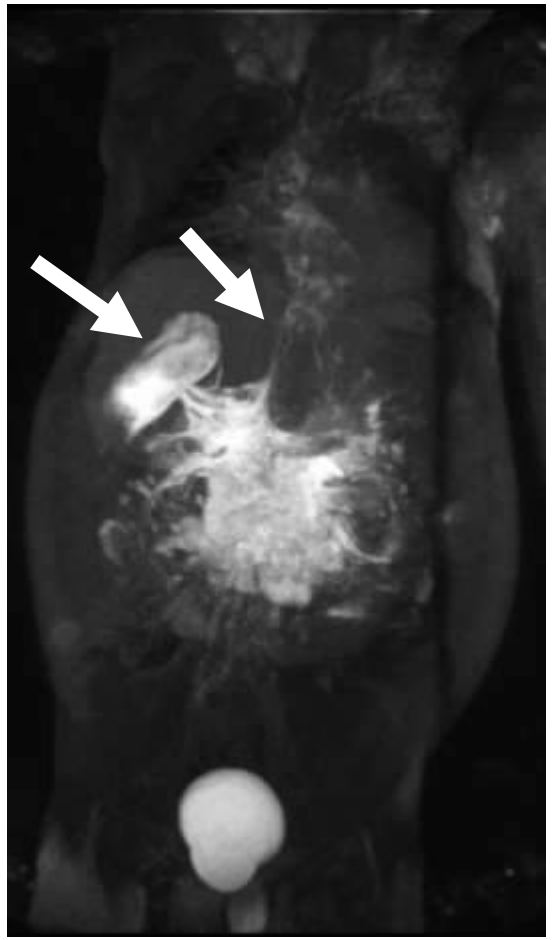


Multicompartment lymphatic failure



T2 Space

IM-DCMRL



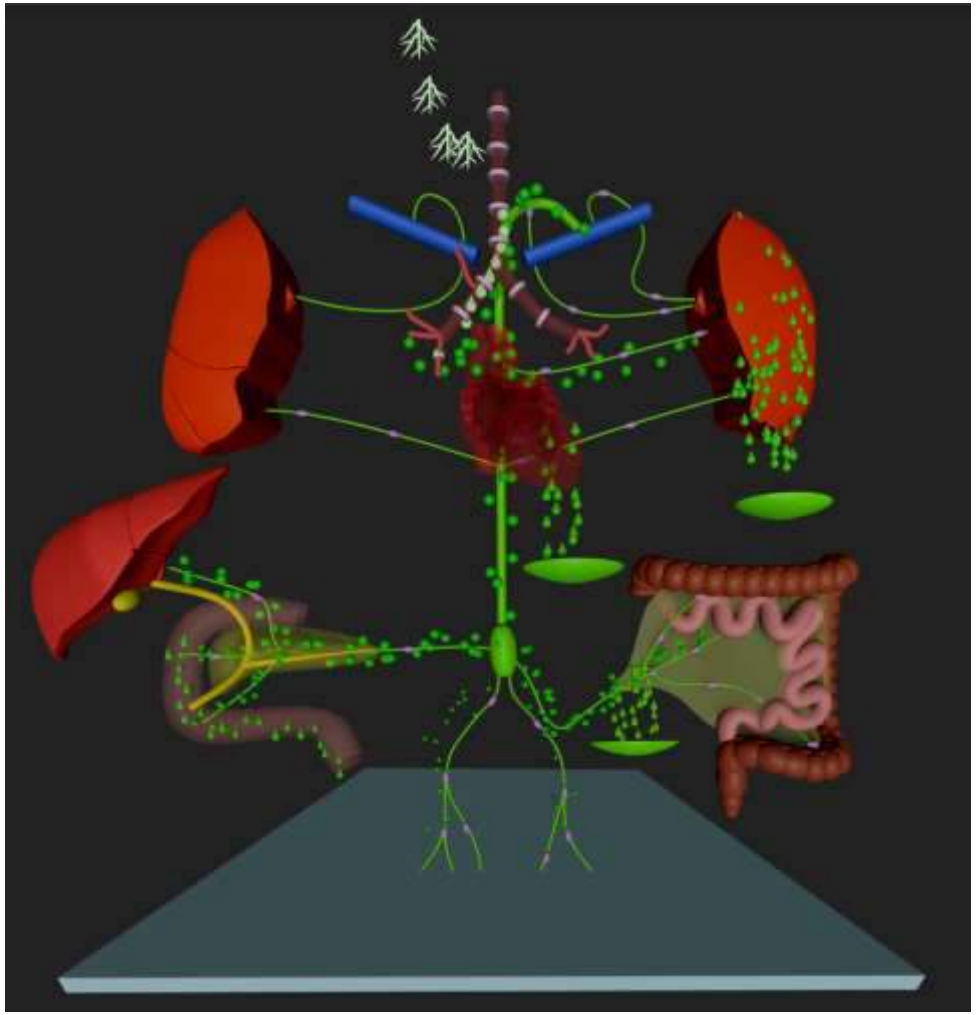
IH-DCMRL

Multicompartment Lymphatic Failure: Initial Treatment

Initial evaluation

- Cardiac Catheterization
  - Hemodynamic assessment
  - Relief of anatomic obstruction

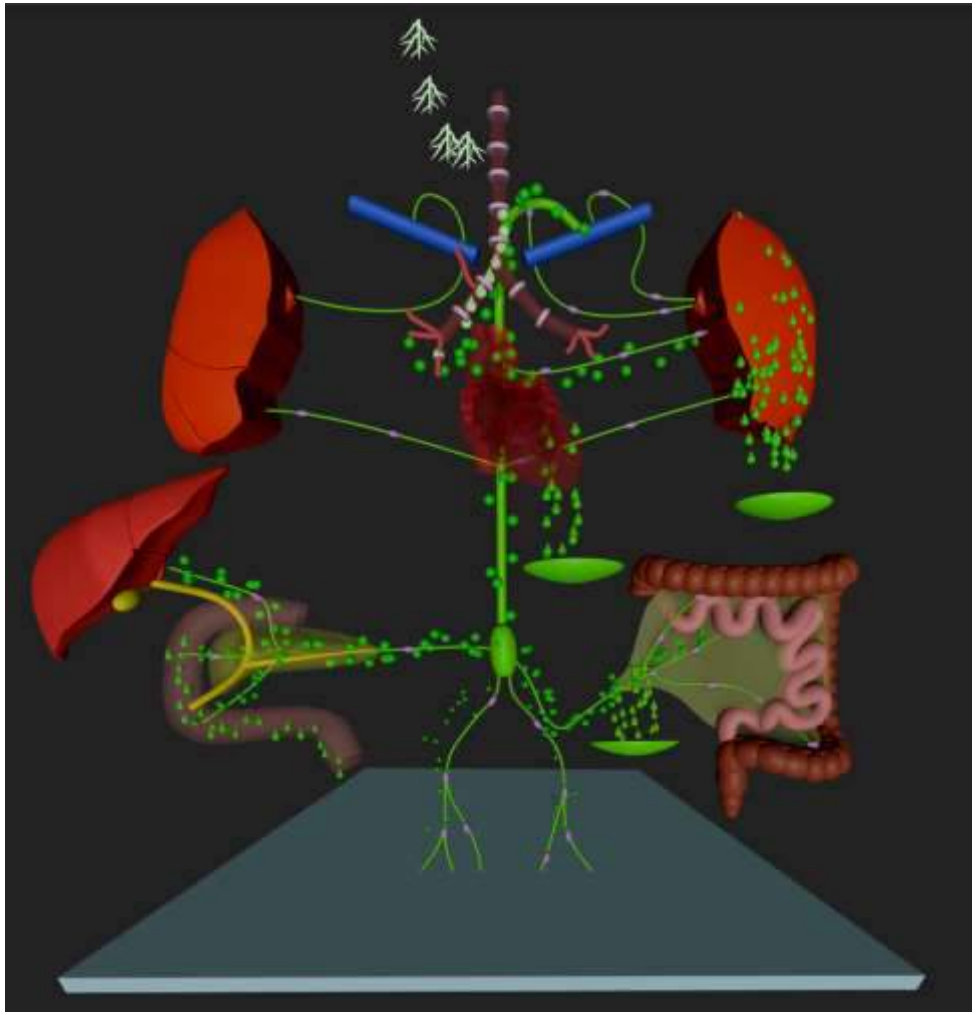
- Medical optimization
  - Sildenafil, pulmonary vasodilators
  - Aldactone
  - Diuretics
  - Compartment specific therapies
  - Additional HF management



Multicompartment Lymphatic Failure: Imaging

Imaging:

- Lymphatic Imaging
  - IN-DCMRL
  - IH- DCMRL
  - IM-DCMRL
  - Assess TD patency



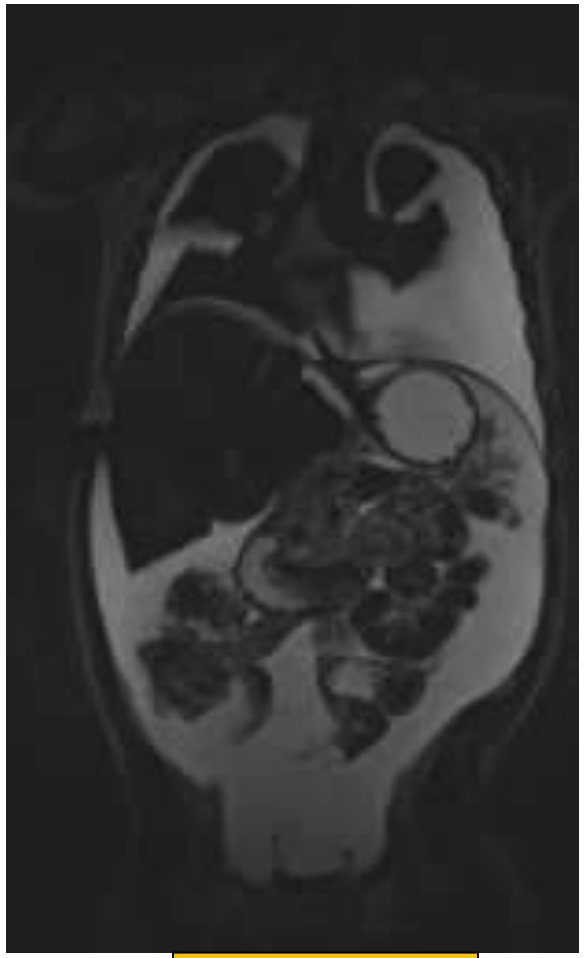
Multicompartment Imaging

IM-DCMRL

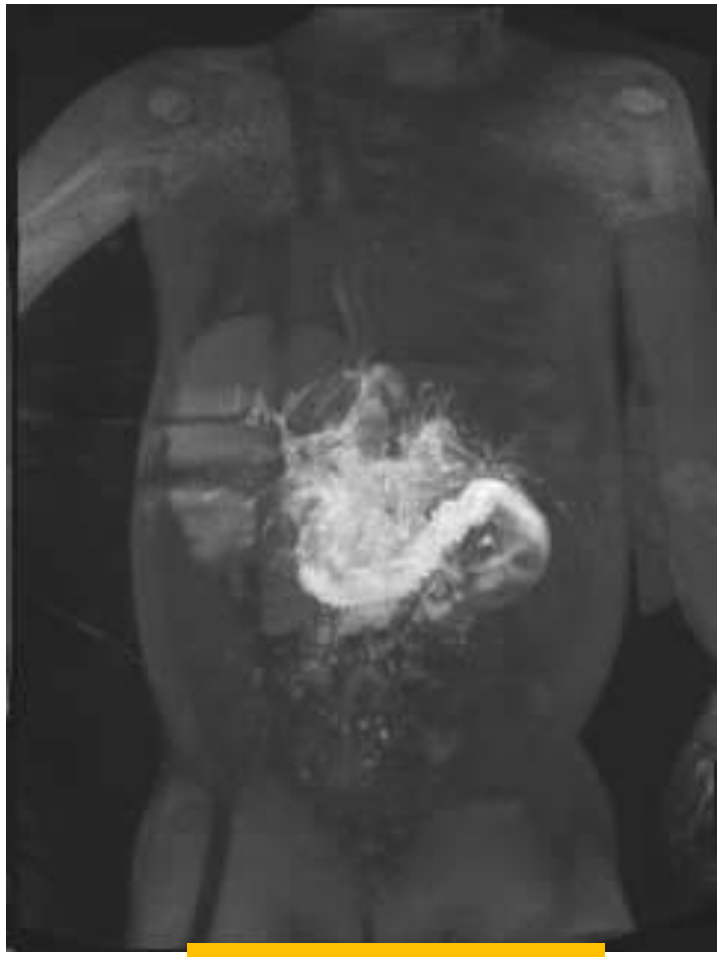
IH-DCMRL

IN-DCMRL

Multicompartment Failure: More than a sum of leaks?



T2 Space



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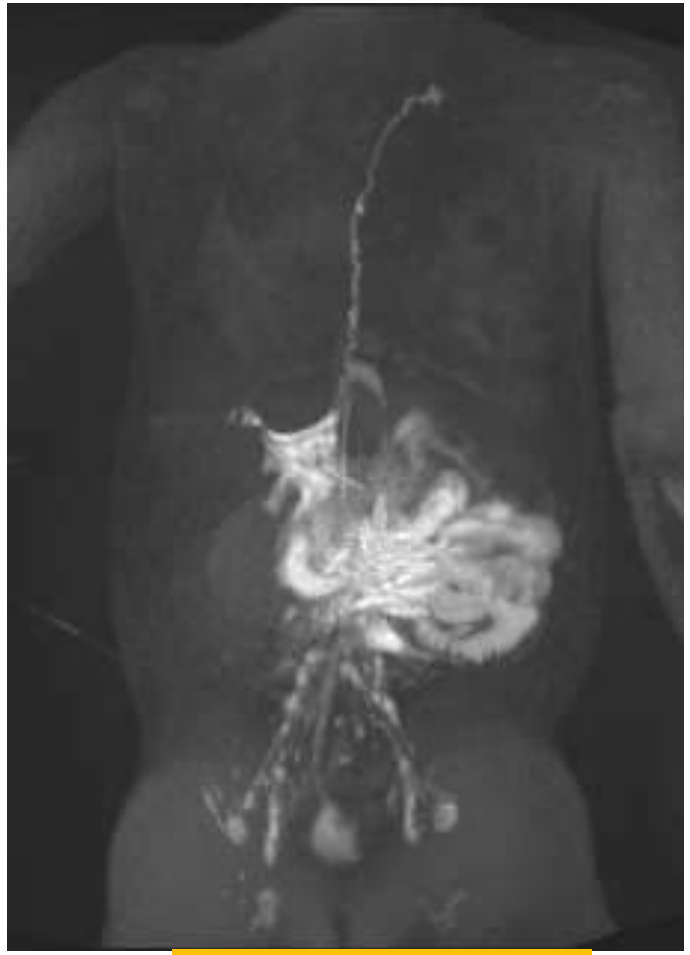

IN-DCMRL

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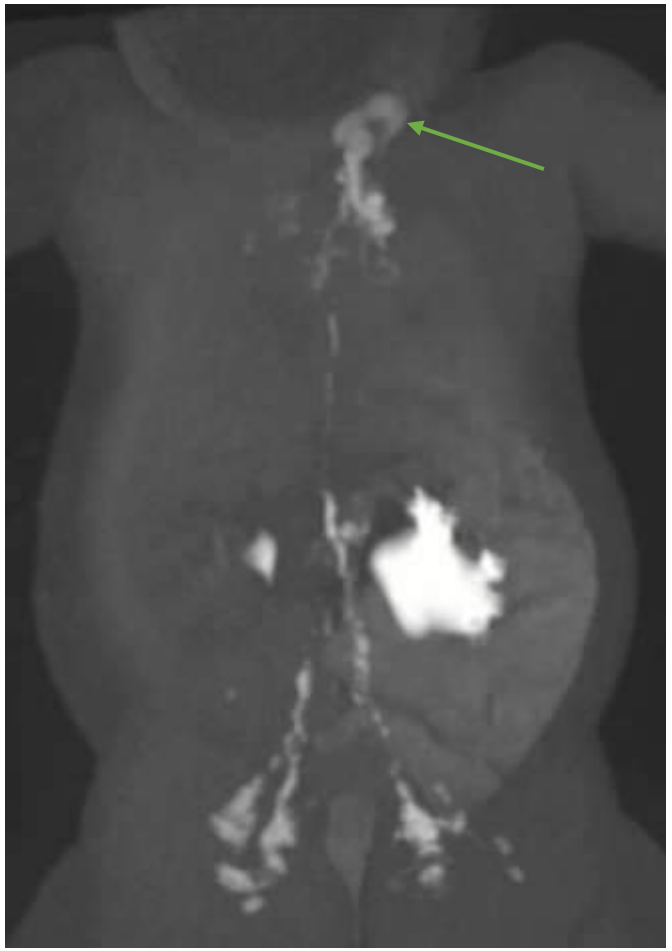
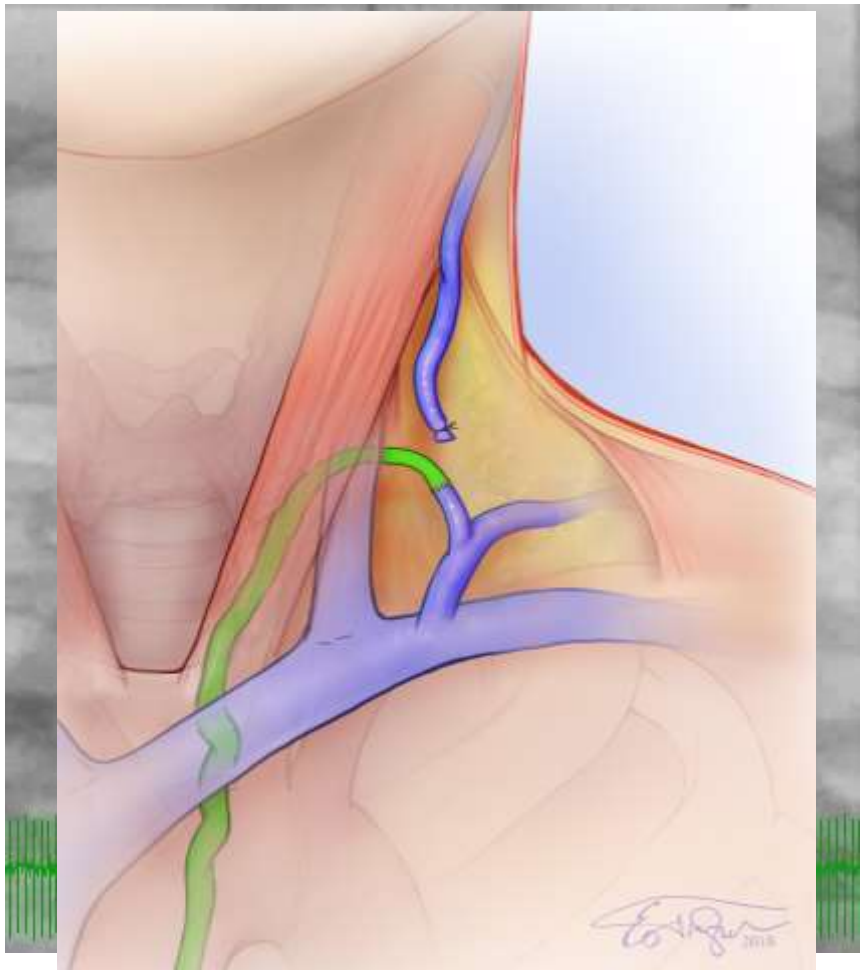
Cardiac Center

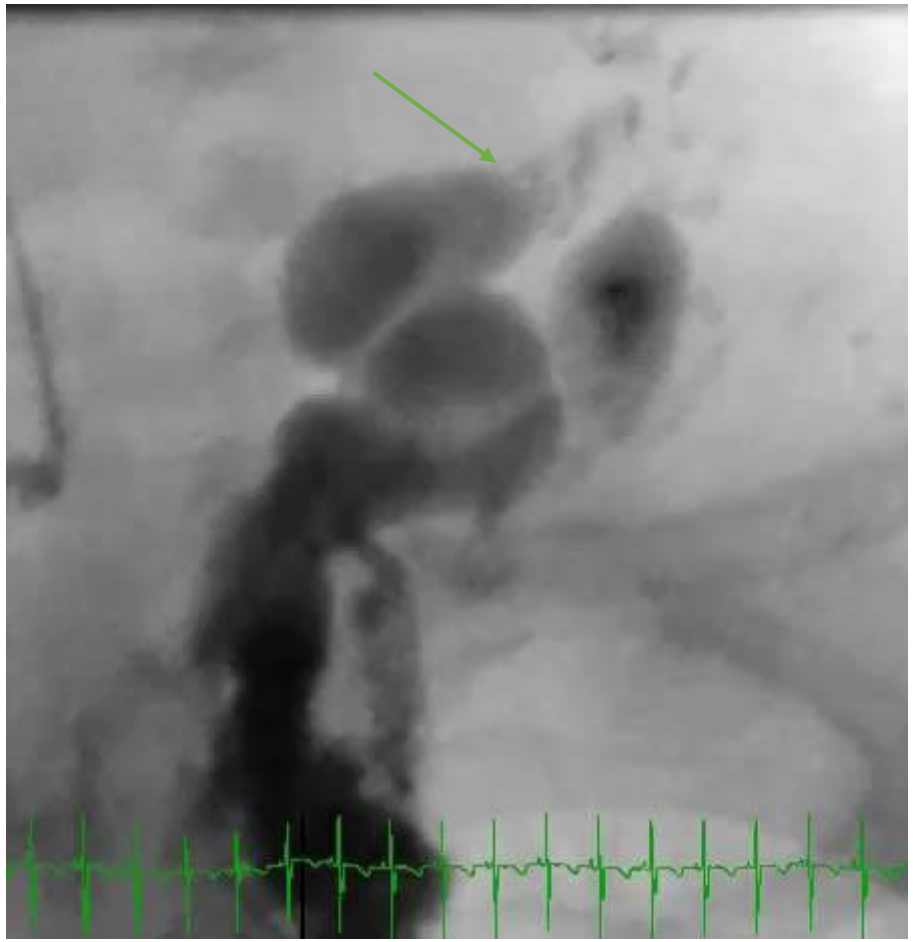
5 mo T21 with CTX, Ascites



IN DCMRL



Lympovenous Ansastomosis



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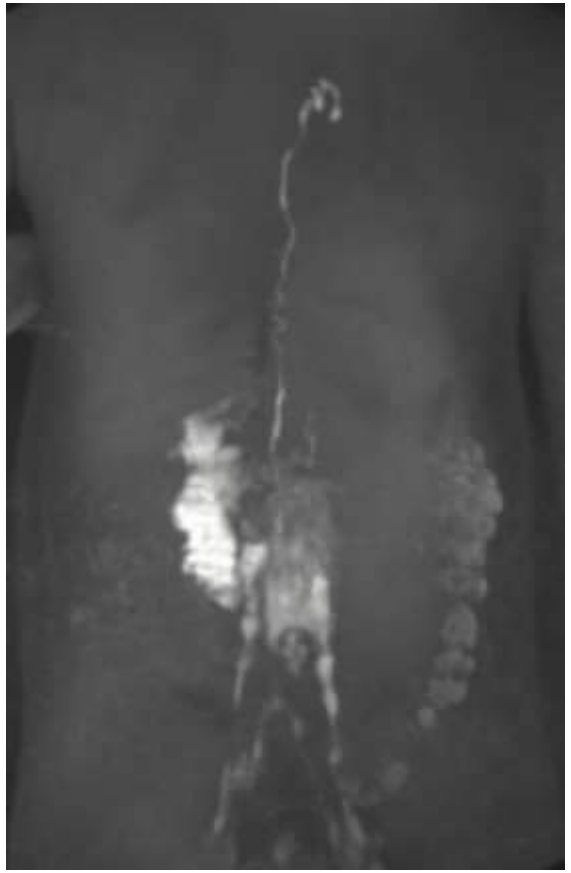
11 y/o Fontan with PLE and Ascites



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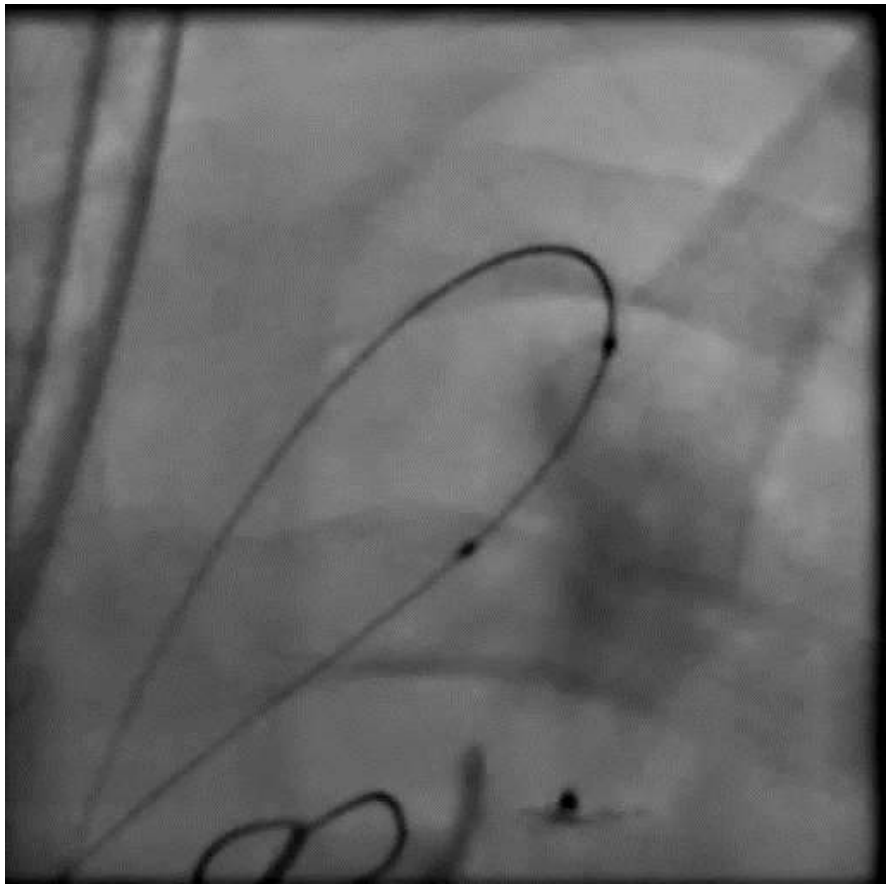

TD = 35 mmHg
InnV = 18mmHg

TD = 22 mmHg
InnV = 20mmHg

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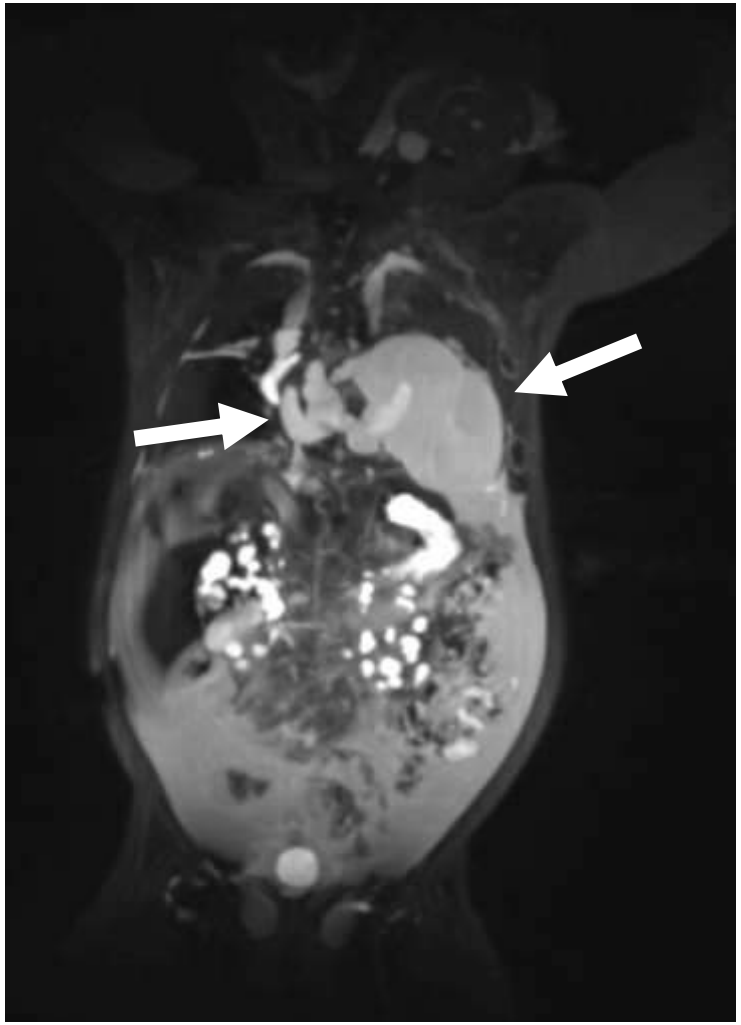
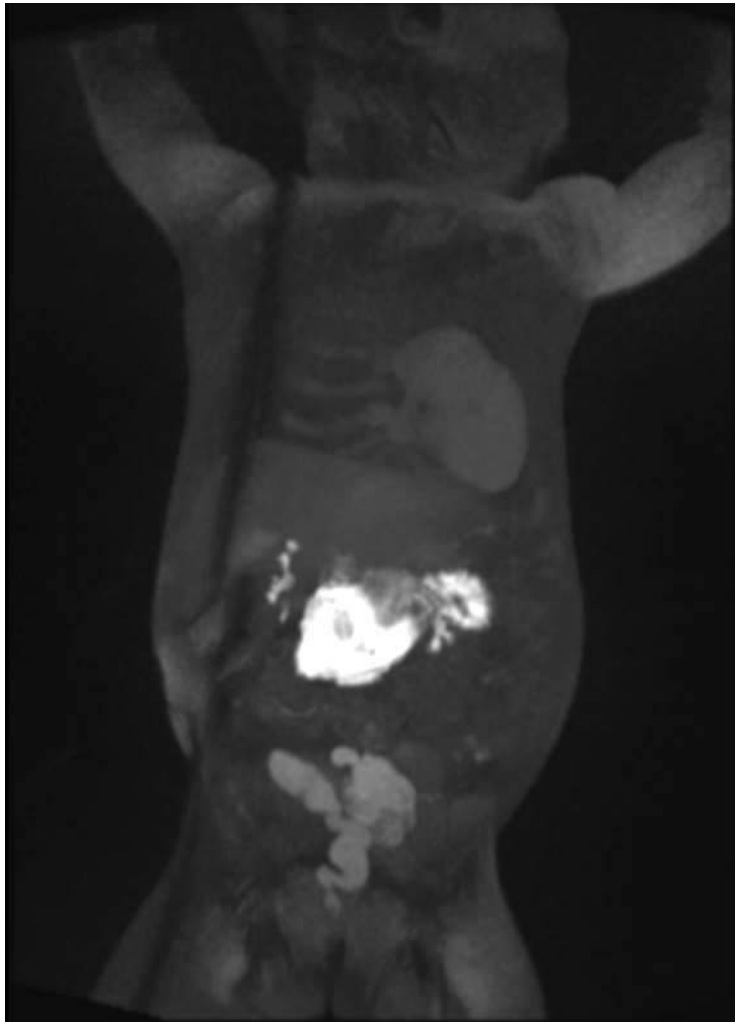
11 mo With GLA PLE and Ascites

T2-MRI



IM-DCMRL



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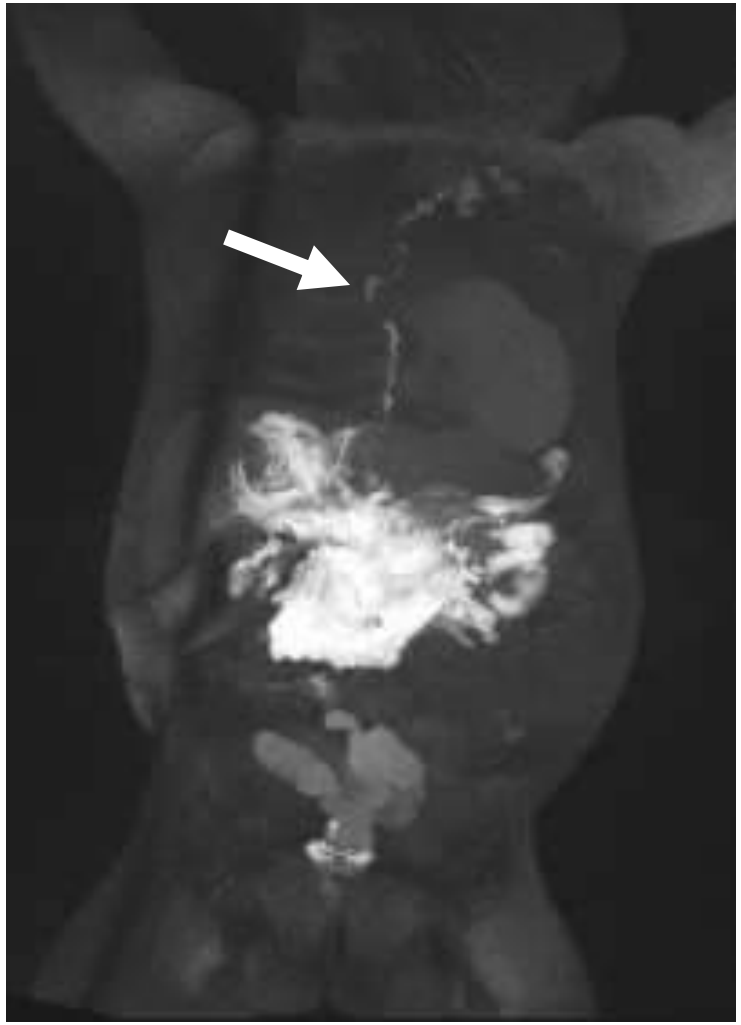
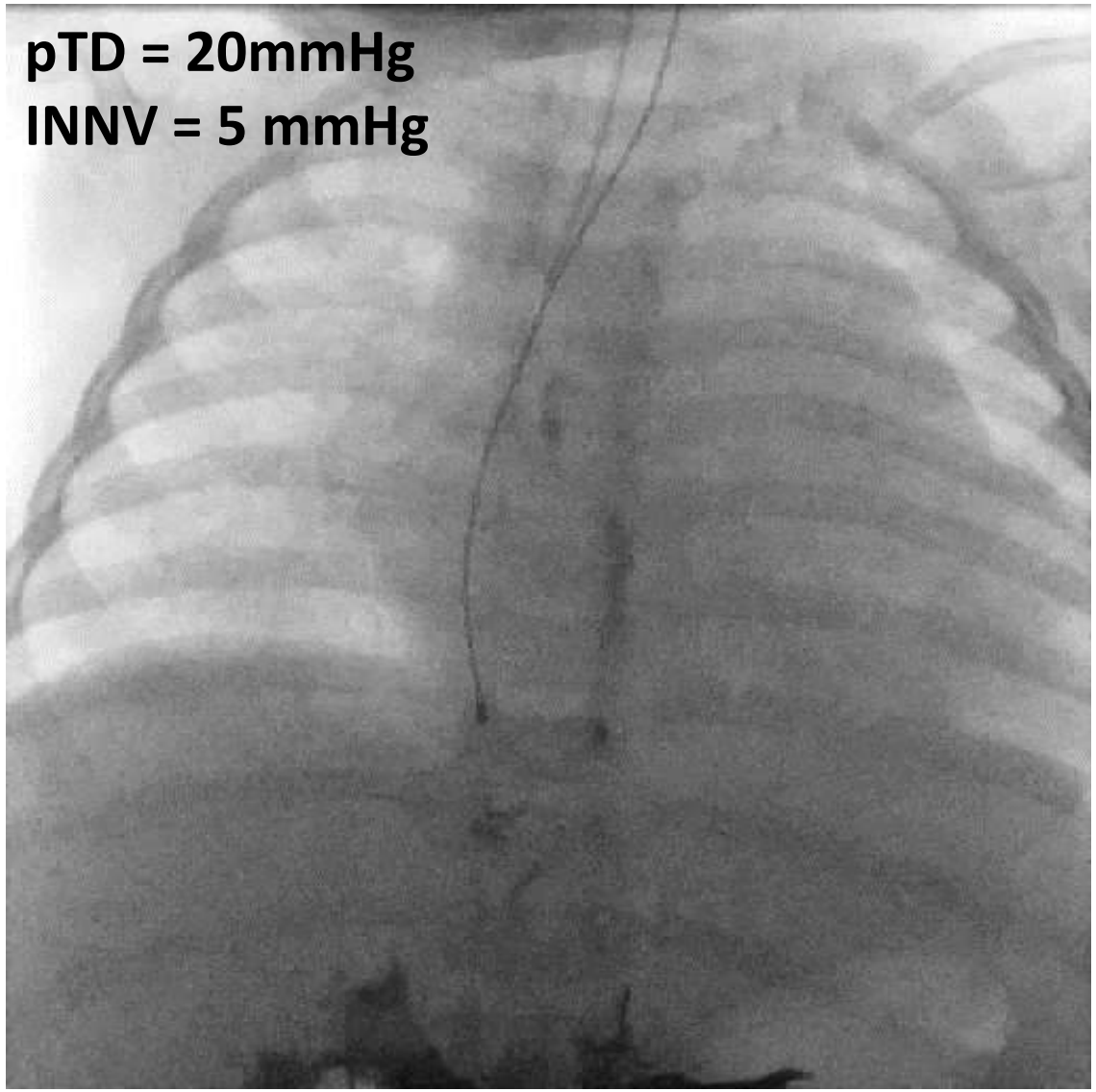
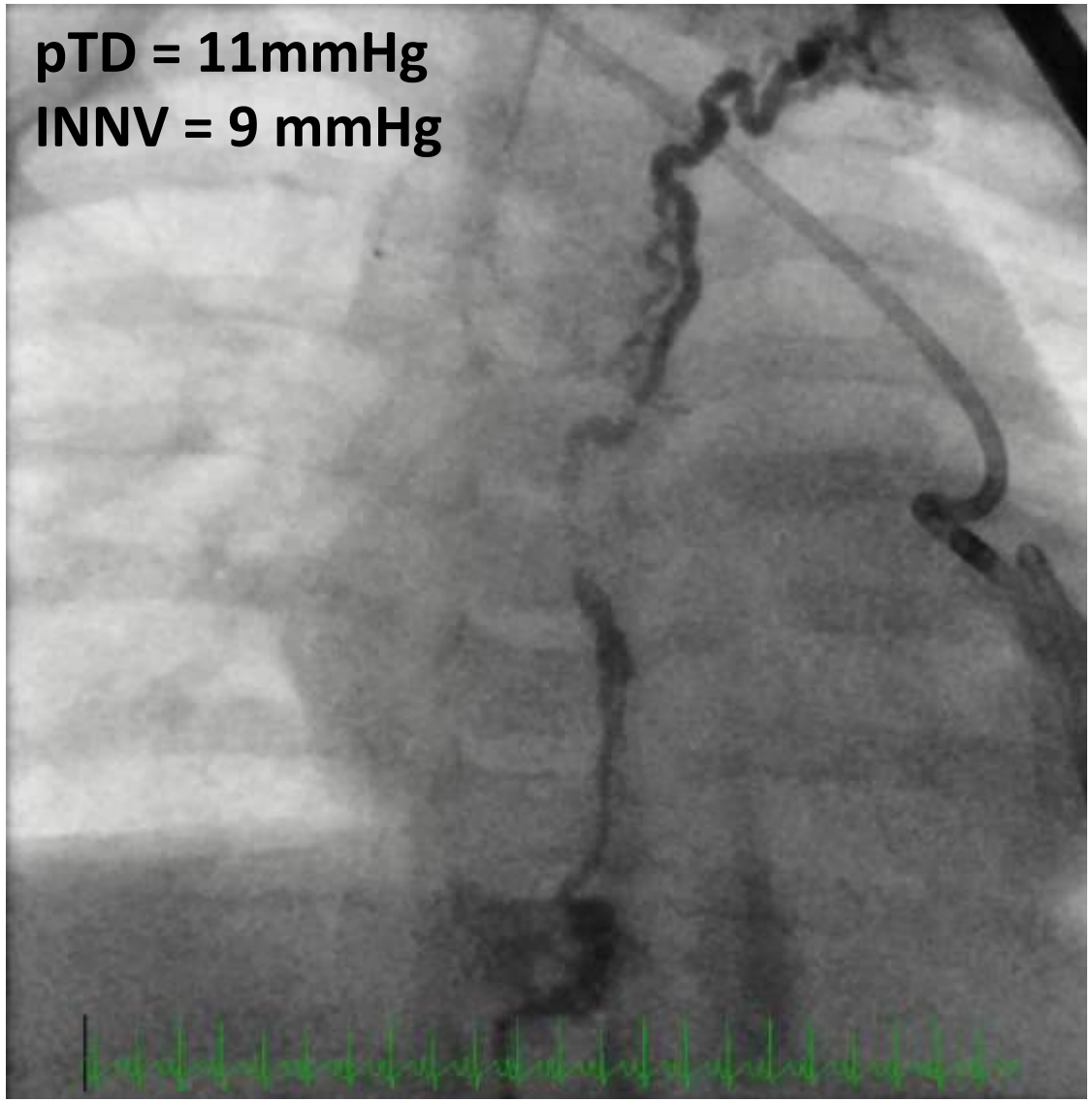
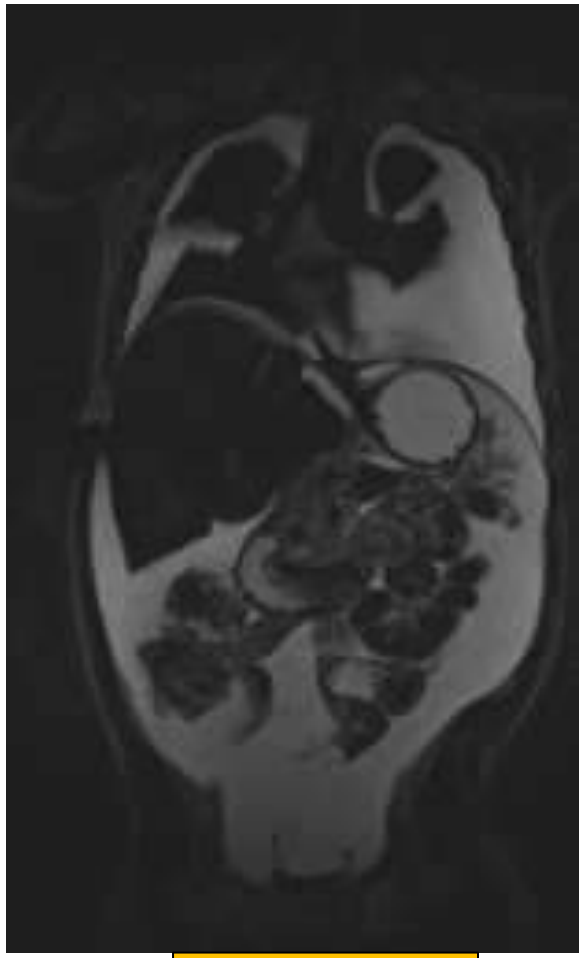


11 mo With GLA PLE and Ascites

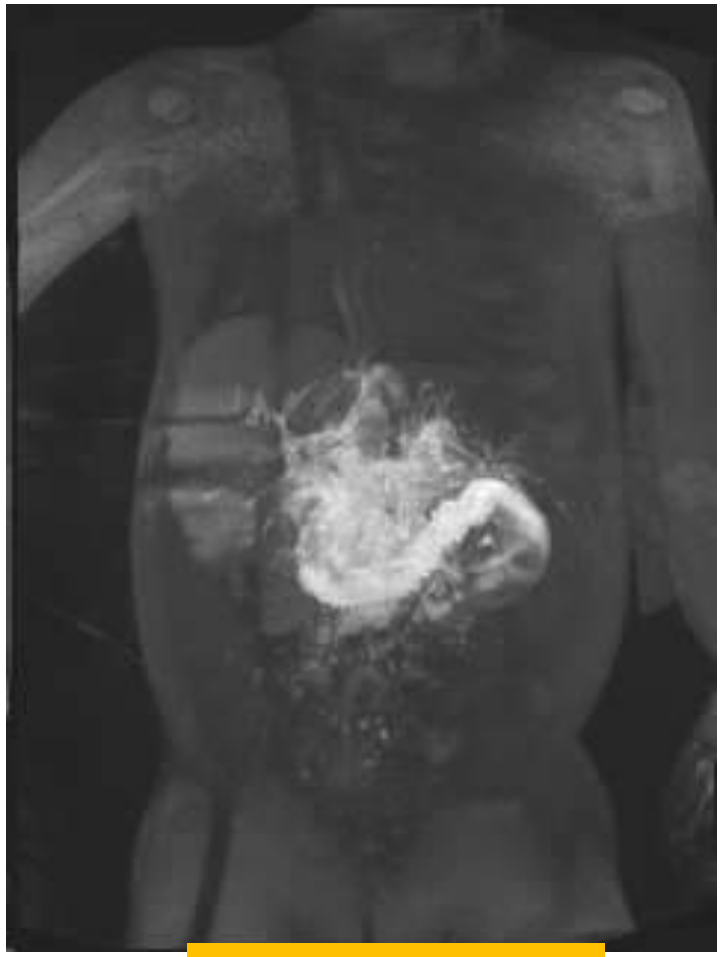




Multicompartment Failure: More than a sum of leaks?



T2 Space



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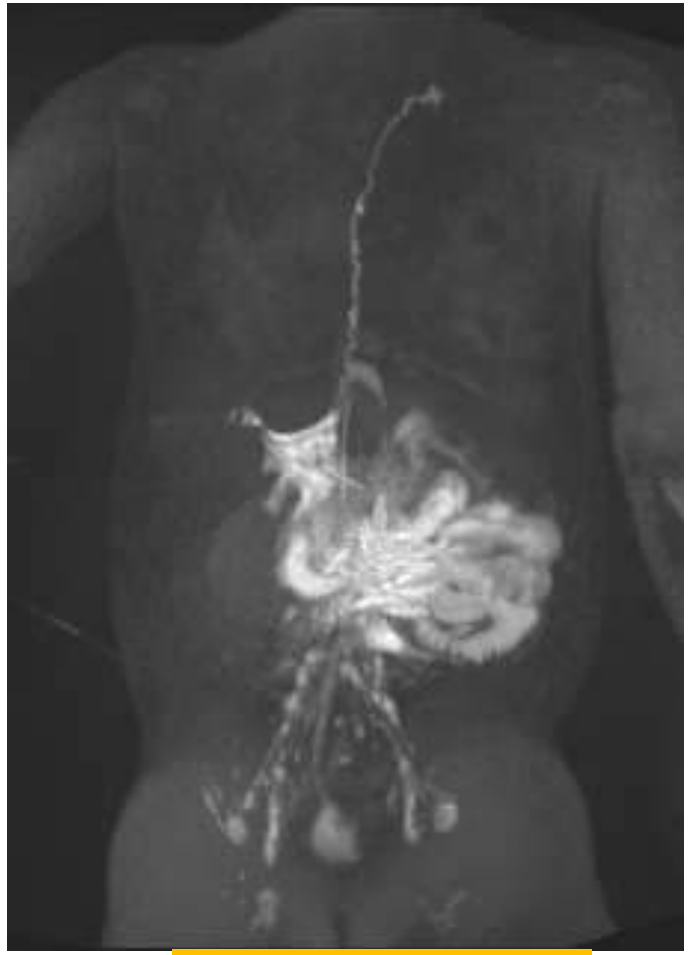

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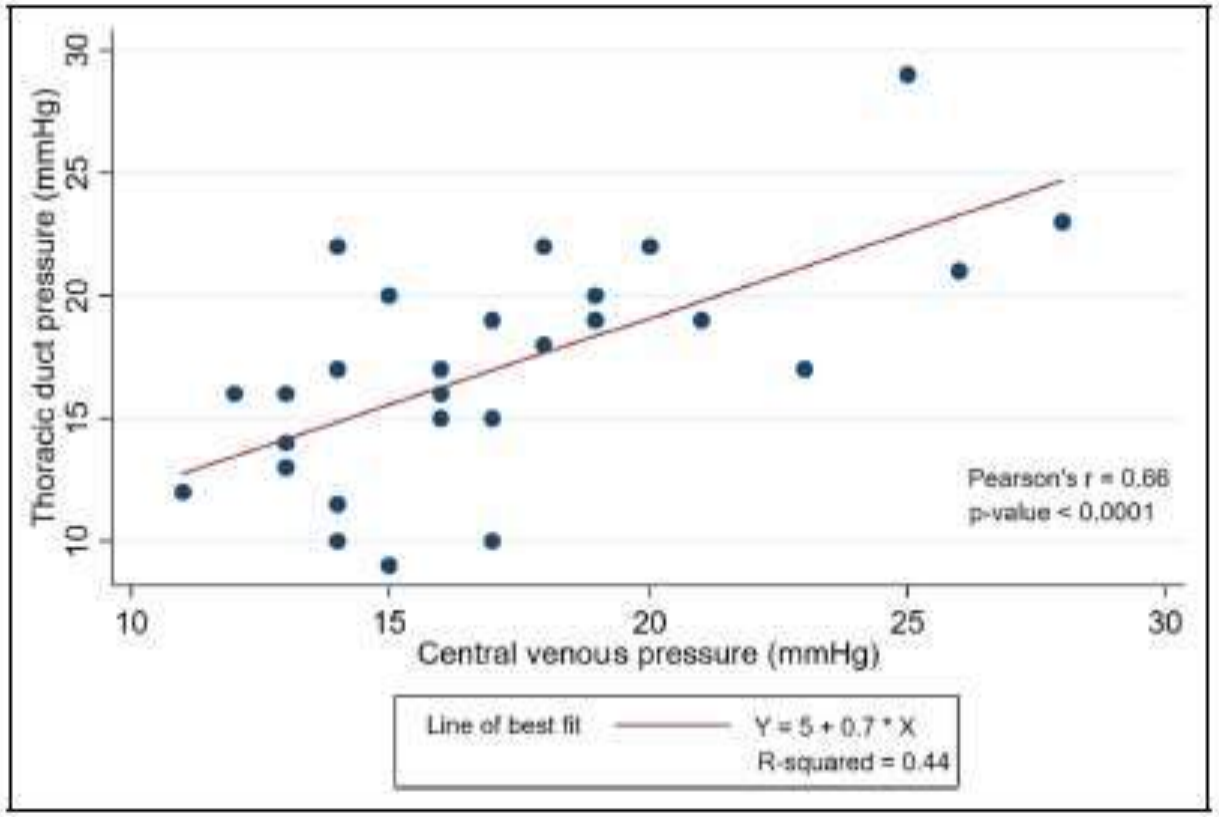

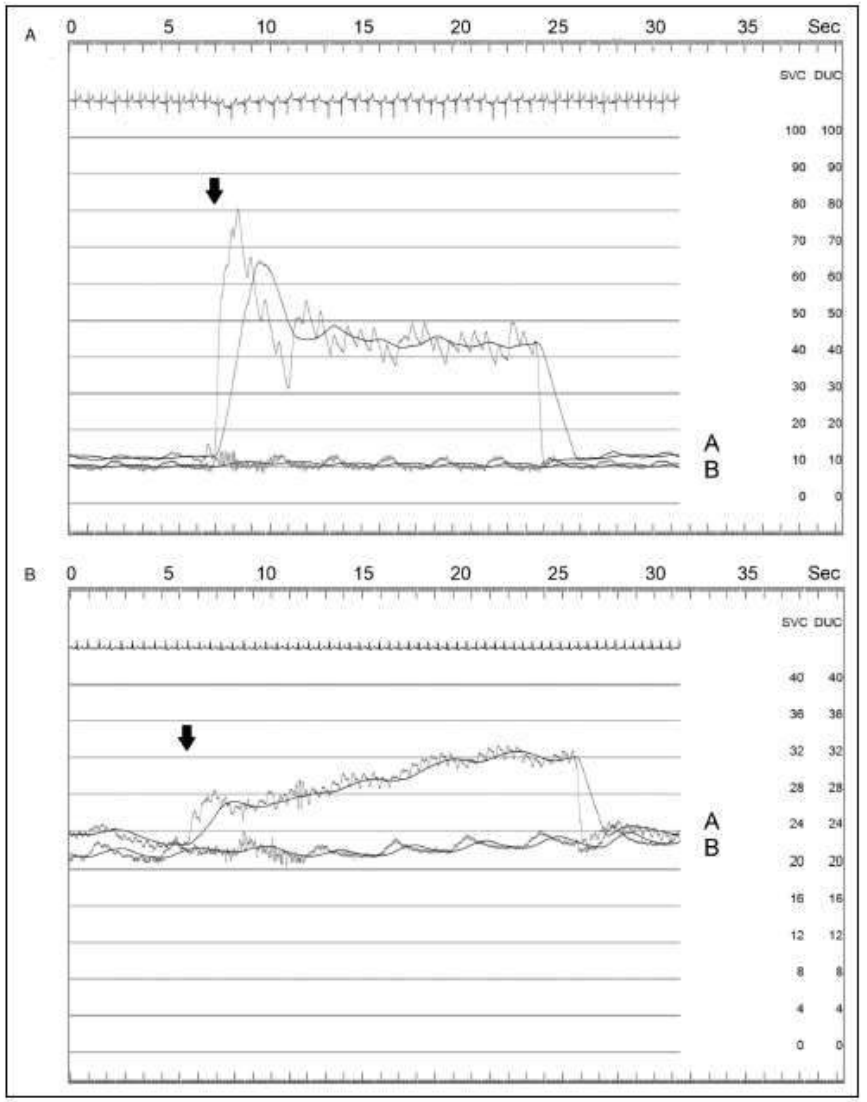

Savla et al. World Journal for Pediatric and Congenital Heart Surgery (Vol 13 (6) 737-744 (2022))

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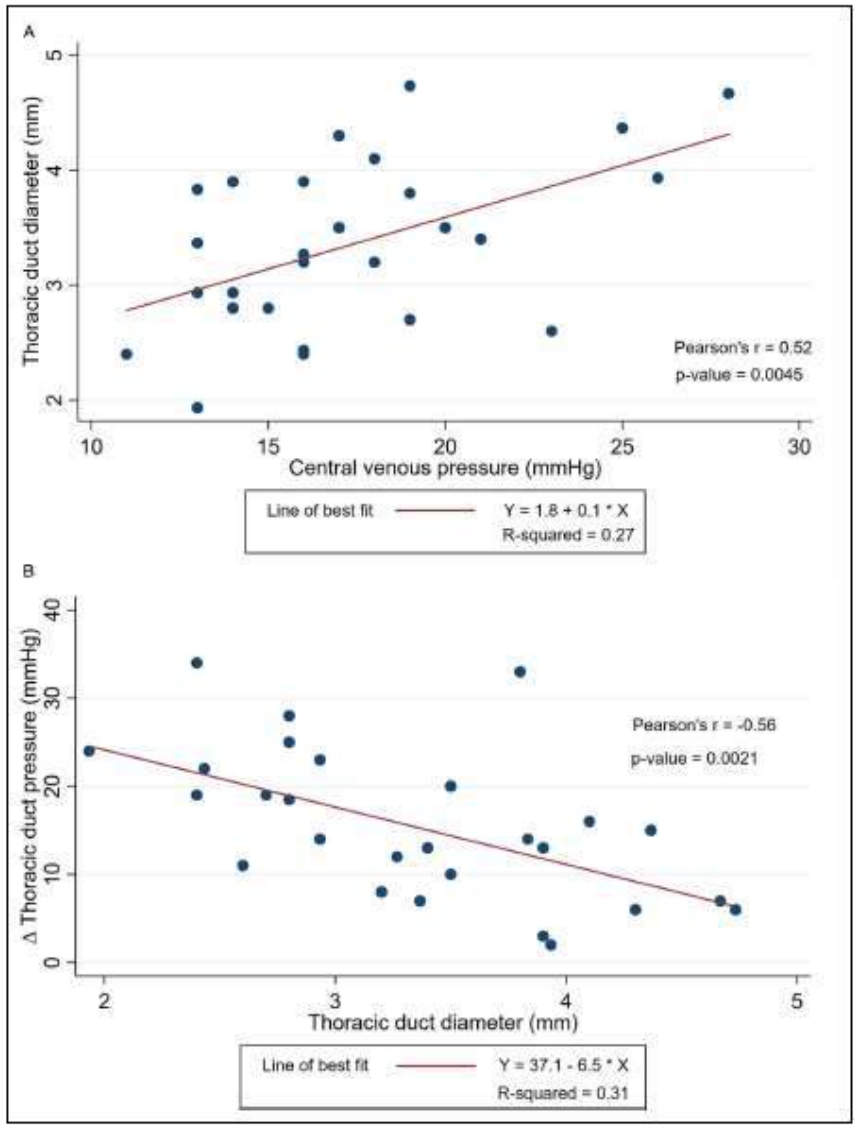

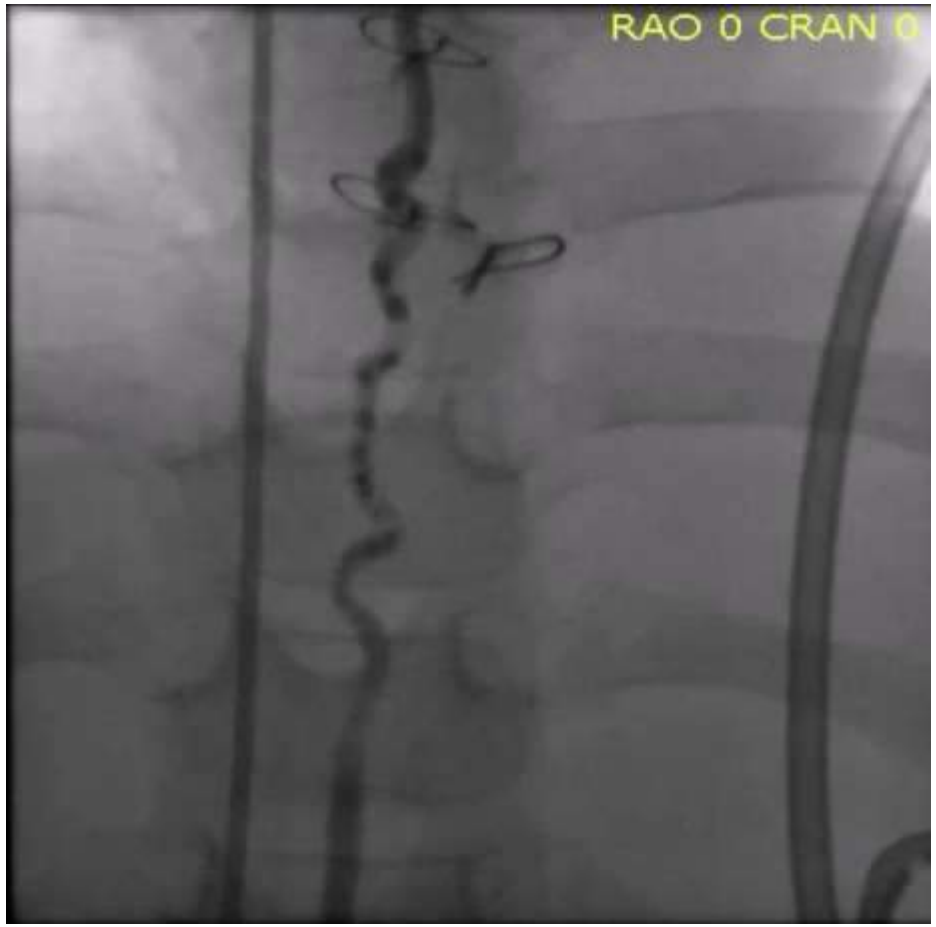

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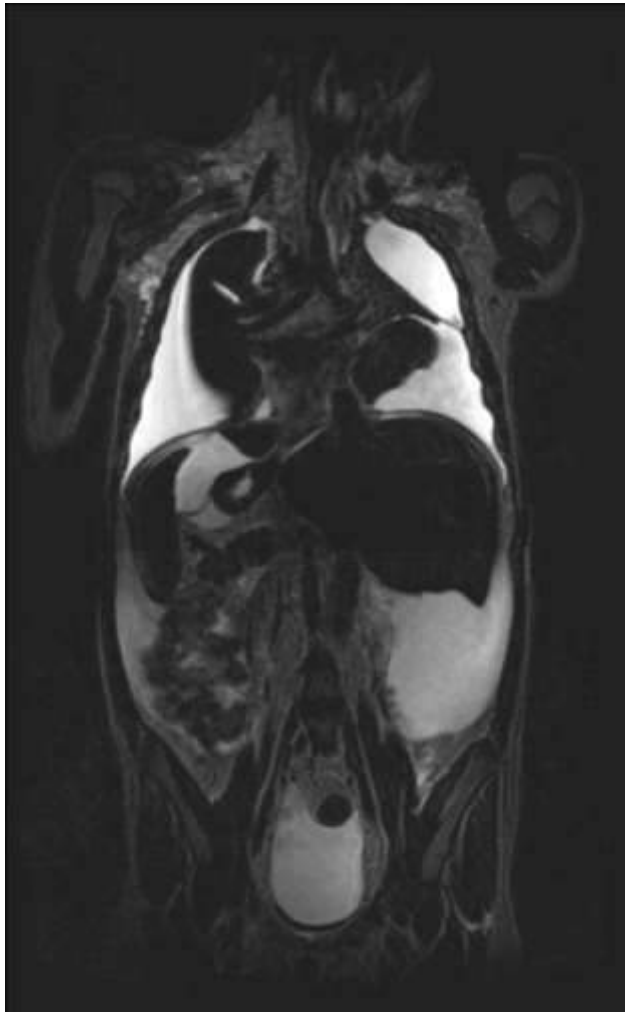
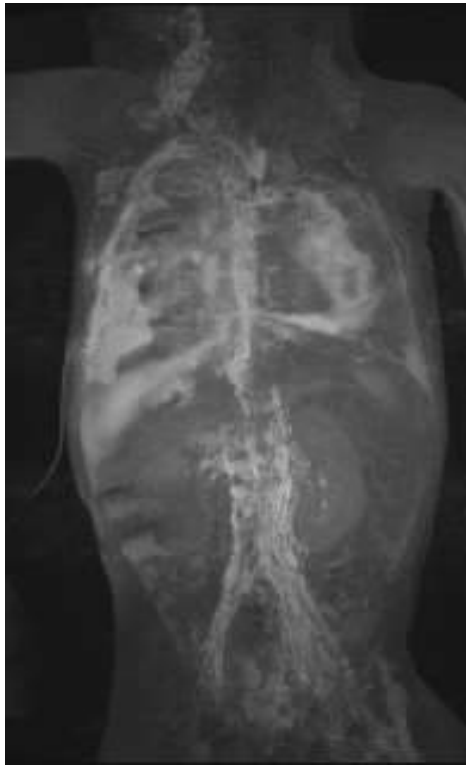
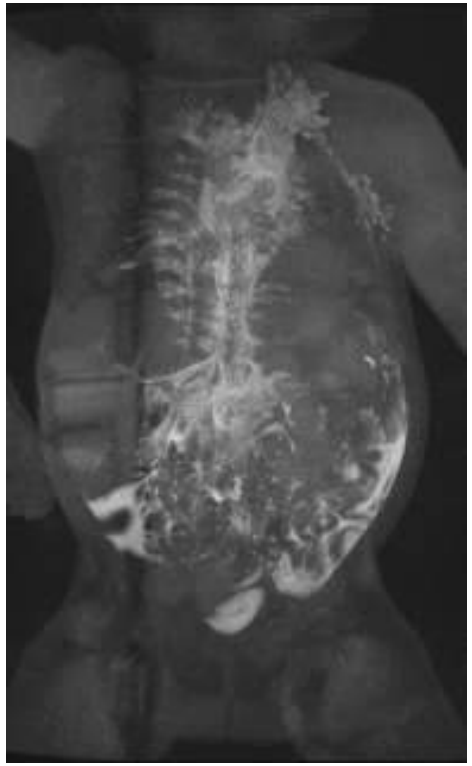






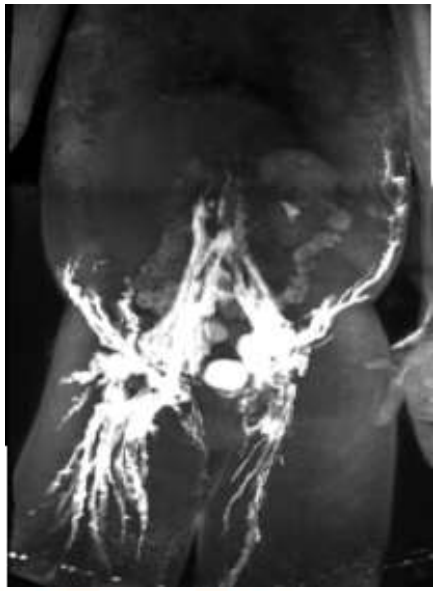
Patient 1: 12 yo with CCLA and ARAF Mutation

Outcome after 3 mo on Trametinib:

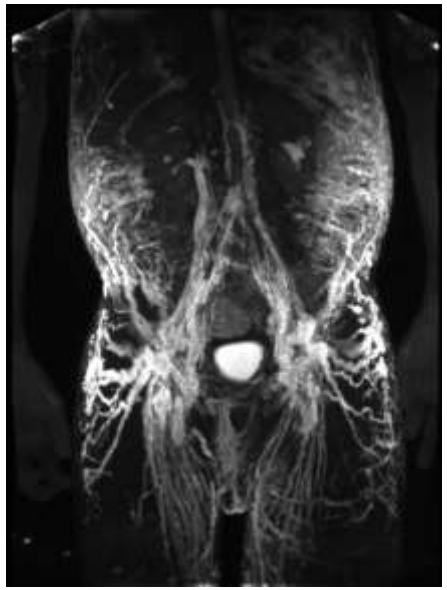
- Doubling of respiratory parameters
- Complete remodeling of central lymphatic system
- Improvement of lymphedema and symptoms

Respiratory Parameter	Baseline (% predicted)	Post Treatment (% predicted)
FEV1 (L)	23	42
FVC (L)	23	40
TLC (L)	29	56
O2 Sat (%)	92	100

DCMRL pre



DCMRL post



Lymphedema pre

Lymphedema post

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(Li et al. Nat. Med. 2019)

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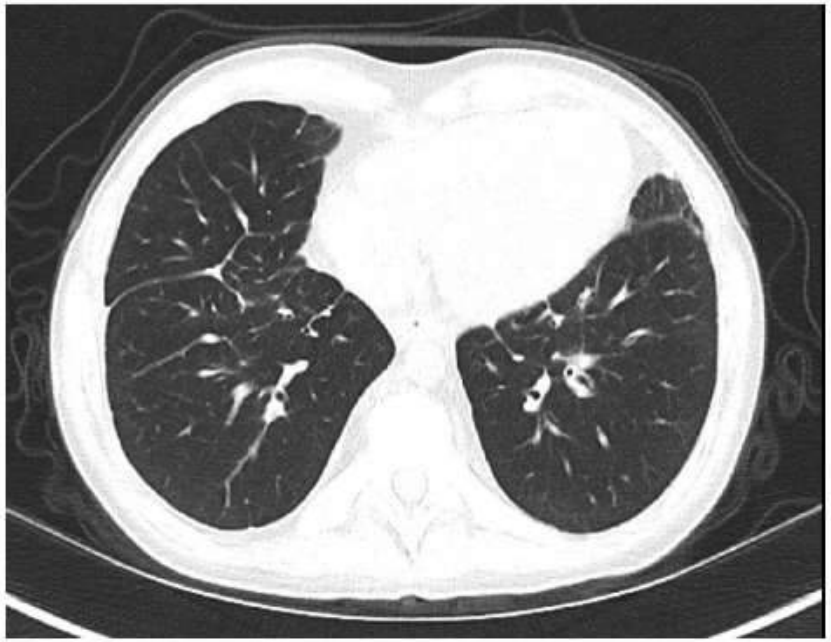
Patient 2: 18 yo with KLA and CBL Mutation

Outcome after 3 mo on Trametinib :

- Normalization of respiratory and clotting parameters
- Complete remodeling of central lymphatic system
- Normalization of chest CT and resolution of effusion

Parameter	Baseline	Post Treatment
FEV1 (% predicted)	53	89
FVC (% predicted)	56	81
TLC (% predicted)	67	87
D-dimer (μg/mLFEU)	9.17	<0.27



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CT pre

CT post

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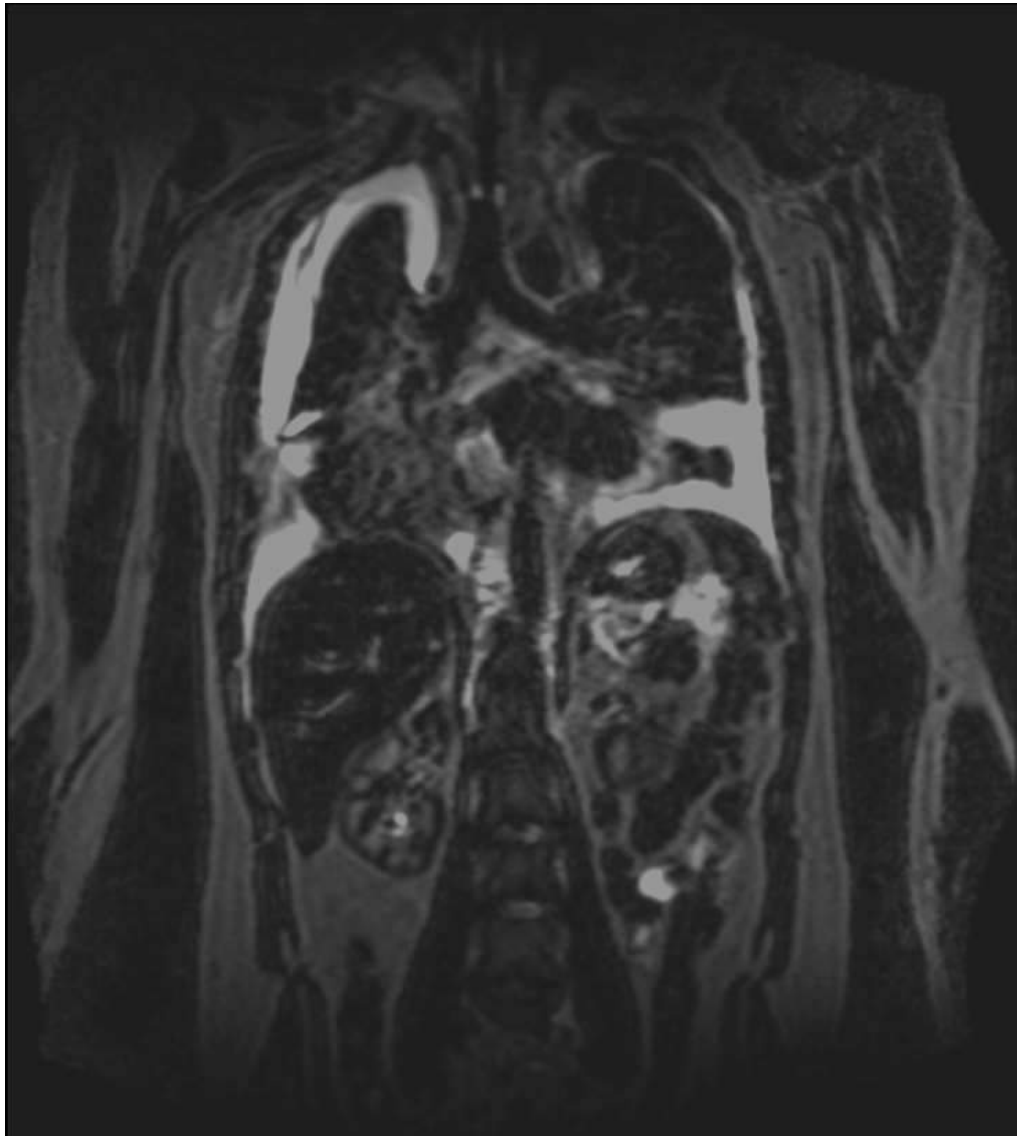
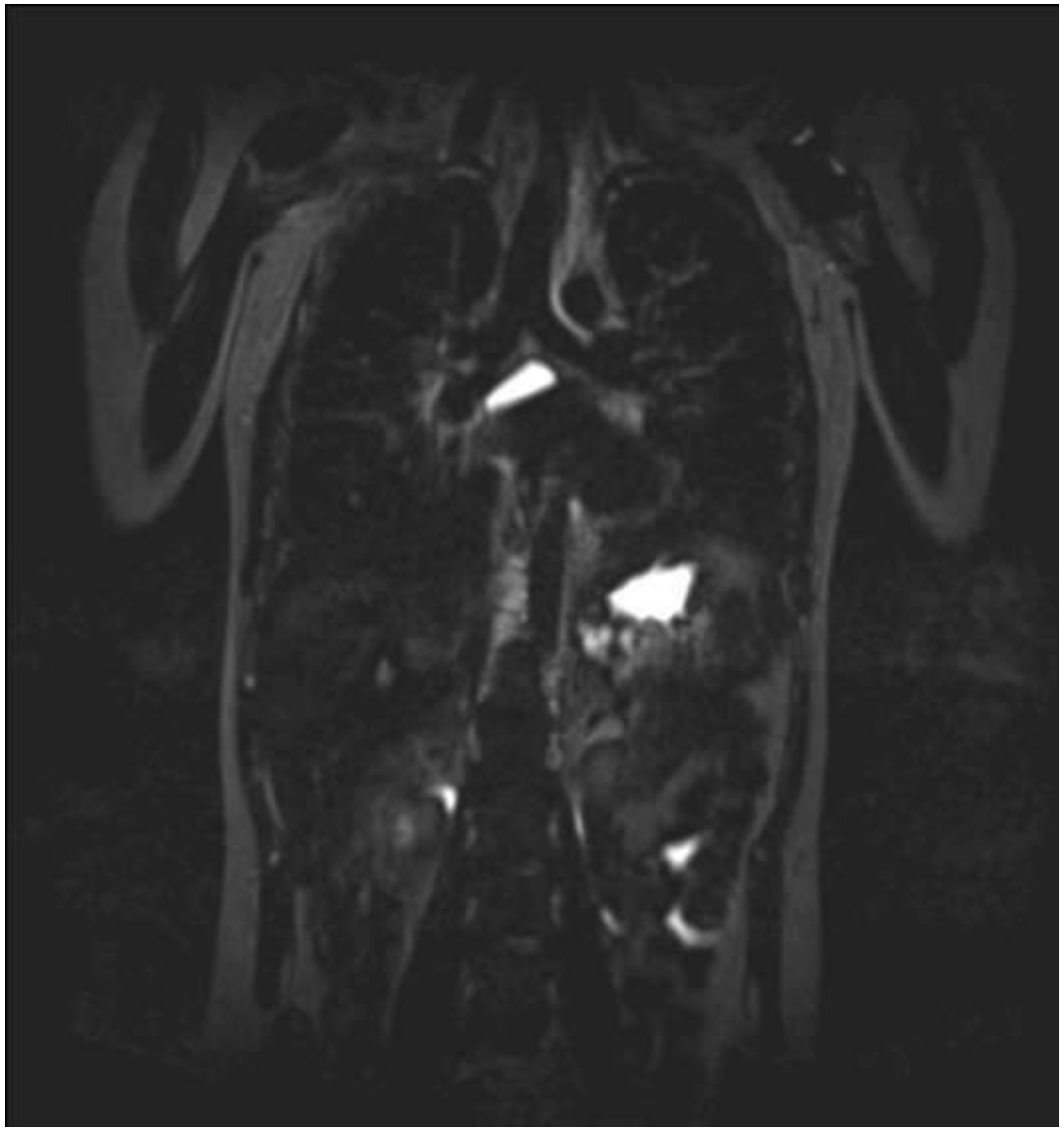
(Foster et al. EMBO Mol. Med. 2020)

Resolution of Pulmonary Edema and Mediastinal Thickening





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T2 pre

T2 post

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Patient 2: 18 yo with KLA and CBL Mutation

Children's Hospital of Philadelphia
Jill & Mark Fishman Center for Lymphatic Disorders

DCMRL pre

DCMRL post

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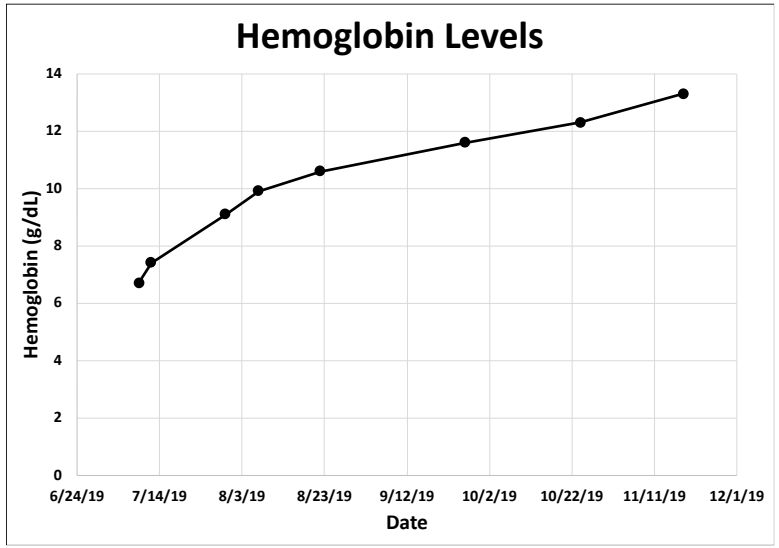
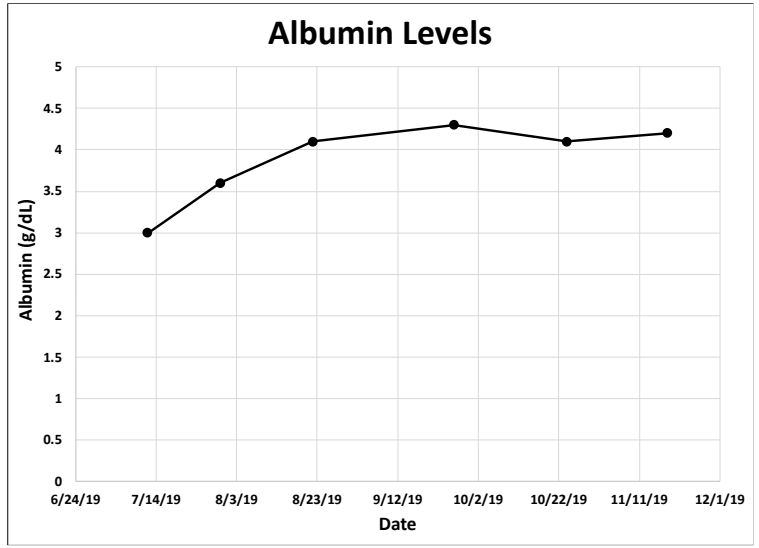
Noonan with SOS1 Mutation and CTx, PLE and UGIB

Trametinib outcome:

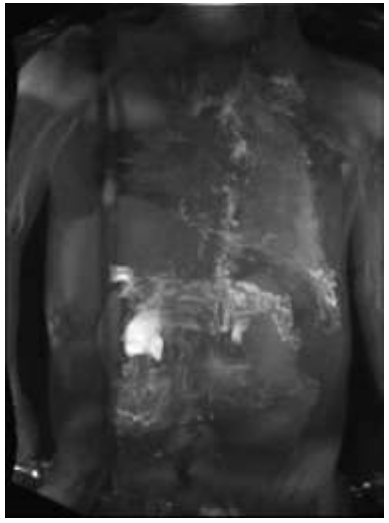
- **Normalization of Hgb and Albumin**
- **Complete remodeling of central lymphatic system**
- **Normalization of duodenal mucosa**





DCMRL pre

DCMRL post



EGD pre

EGD post

Dori et al

Summary

Keys to diagnosis and treatment of multicompartment failure

- Multicompartment imaging is necessary
- Evaluate for global causes (i.e. obstruction)
- Focus on selective embolization, but recognize other compartments may worsen
- Not all multicompartment failure is the same
- Consider targeted medical therapies if underlying genetic cause
- **Do not ligate the thoracic duct** in patients with multicompartment failure
  - Advanced therapies to modify underlying lymphodynamics