Radiofrequency Ablation of Aldosteronomas (Conn’s Syndrome): A New Application of IR

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Mayo-Smith W W et al. Radiographics 2001;21:995-1012

Dupuy D E et al. Radiographics 2002;22:S259-S269
Outline

- Patient Presentation
- Differential Diagnosis
- Living Anatomy
- Menu of Radiologic Tests/Imaging Algorithm
- Diagnostic Interventions
- Therapeutic Interventions
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48yo M presents with refractory hypertension associated with hypokalemia since age 30.

PMH: none

Fam Hx: noncontributory

Meds: HCTZ, Amlodipine, Terazosin, Metoprolol, K supplement
Indications for Secondary HTN Screening

- Severe or **refractory**
  - (Refractory to 3+ bp meds)
- **Negative family history**
- Acute rise in bp or creatinine
- Onset <puberty or >50
- Asymmetry in renal disease
- Abdominal bruit.

Kaplan, Rose. Screening for Renovascular or Other Causes of Secondary Hypertension. UpToDate. 2010; 18.3

Source: Dong Q et al. Radiographics 1999;19:1535-1554
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Differential Diagnosis of Secondary Hypertension

Common

- Primary Aldosteronism (PA)
  - Present in up to 10% patients with hypertension
- Primary Renal disease
- Renovascular Hypertension (RAS)

Uncommon

- Pheochromocytoma
- Cushing’s syndrome
- Coarctation of the Aorta
- (Other): Obesity, Alcoholism, Sleep apnea
- Reninoma

Patient 1’s Initial Workup

- The first step in his workup for secondary hypertension was a renal doppler ultrasound.

- Images from this ultrasound were unavailable, but similar images in a patient with the same diagnosis will be described on the next slide.
Companion Patient 1: Renal Doppler US
Shows no evidence of RAS

- US assesses renal arteries anatomically and functionally
- Best indicator of RAS is increased peak systolic velocity

This raises the question: is a renal doppler ultrasound indicated in the initial work-up of a patient with refractory hypertension?
ACR Appropriateness Criteria

- Renal doppler US is an *inappropriate* first step in the evaluation of secondary hypertension.

- Renovascular HTN is **not** the most common cause of secondary HTN.

Even if Renovascular HTN suspected:
- C+ MRA and/or CTA ➔ Rating of 8
- US Kidney + Doppler ➔ Rating of 6

Kahn, S. Techniques in Vascular and Interventional Radiology 2010; 13.2: 110-125

Patient 1 MRA: No evidence of RAS

Source: BIDMC, PACS Courtesy of Dr. Knutson

Patent Renal Arteries bilaterally

Accessory Left Renal Artery

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Patient 1 MRA: Incidental Adrenal Nodule

Left Adrenal Mass:

Source: BIDMC, PACS
Outline

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Origin of the Adrenals (Embryology)

Adrenals in the body (Gross Anatomy)

- Diaphragms
- Adrenals
- Kidneys

Adrenals on MRI (Living anatomy)

Adrenals: wispy, y-shaped, low signal masses

Source: BIDMC, PACS Courtesy of Dr. Knutson

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Adrenal Mass: Etiologies

Benign Lesions
- Cysts
- Myelolipomas
- Sequelae of previous trauma
- Adrenal Hyperplasia

Benign Neoplasms
- Pheochromocytoma
- Adenomas
  - nonfunctioning
  - hormone-secreting

Malignant Neoplasms
- Metastases
- Lymphoma
- Adrenocortical carcinoma
- Angiosarcomas
- Neuroblastoma

Source: http://healthpictures.com/images/Pheochromocytoma.jpg
Not So Fast!!! “Pseudolesions” include:

- **GI**
  - Gastric diverticulum
  - Gastric fundus
  - Dilated colon

- **Reticuloendothelial**
  - Hepatic mass
  - Splenules
  - Splenic lobulations

- **Vascular (noncontrast)**
  - Varices
  - Splenic, Renal a. aneurysm

Source: BIDMC, PACS Courtesy of Dr. Knutson

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Adrenal Gland: Menu of Radiologic Tests

- **CT +/- contrast**
  - Modality of choice for initial characterization of adrenals but is nonspecific for masses
  - 3-Phase (delayed contrast) CT evaluates washout characteristics of adrenal masses

- **MRI +/- contrast**
  - Better soft tissue differentiation
  - Chemical Shift imaging evaluates lesions not adequately characterized by CT

- **Radiography**
  - Fluoroscopy-guided procedures

- **Less Commonly used tests:**
  - **Ultrasound**
    - Only readily identifies large masses
  - **Nuclear Scintigraphy**
    - I-131 meta-iodobenzylguanidine (MIBG) assesses medullary function
    - I-131 6-beta-iodomethyl-19-norcholesterol (NP-59) assesses cortex
C- CT is nonspecific for Adrenalomas

- In majority of adenomas, CT is inaccurate or noncontributory.

- On CT, Adenomas are:
  - Small → but can be large (4-6cm)
  - Homogenously enhancing → or heterogenous if hemorrhage
  - Lipid-rich (HU<10) → or up to 25HU if lipid-poor

- 3 Phase C+ CT increases specificity:
  Adenomas demonstrate rapid washout (APW >60%, RPW >40%) → but not absolute, requires contrast administration
3-Phase CT: calculating APW, RPW

- “Washout” = Comparison of Attenuation Measurements during 3 phases of C+ CT
  - 1- Precontrast
  - 2- Portal Venous
  - 3- Delayed phase

- Absolute Percent Washout = $\text{APW} = \frac{X}{Y}$

- Relative Percent Washout = $\text{RPW} = \frac{X}{\text{HU}_{\text{Portal Venous Phase}} - \text{HU}_{\text{Precontrast Phase}}}$
  - $\text{HU}_{\text{Portal Venous Phase}} - \text{HU}_{\text{Precontrast Phase}} = Y$
  - $\text{HU}_{\text{Portal Venous Phase}} - \text{HU}_{\text{Delayed Phase}} = X$

- Typically, Adenomas have $\text{APW} > 60\%$ and $\text{RPW} > 40\%$

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Imaging Algorithm for Adrenal Incidentalomas

C- CT

HU>10

Delayed C+ CT

HU>30
APW<60%
RPW<40%

Biopsy

HU<30
APW>60%
RPW >40%

Benign

MRI w shift

Signal Dropoff

Benign

No Signal Dropoff

Biopsy

Benign

Benign

Benign

Benign
The Imaging Algorithm for Adrenal Incidentalomas is not useful in Patient 1’s case, as he had an MRA before CT.

Let’s return to his MRA in attempts to further characterize his adrenal mass.
Our Patient: Incidental Adrenal Nodule on MRA

Left Adrenal Mass:

Source: BIDMC, PACS
Our Patient: Shift Imaging reveals adenoma

Out of Phase MRI

In Phase MRI

Source: BIDMC, PACS

Low signal mass

Lower signal, similar to spleen

Source: BIDMC, PACS

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**MR Chemical Shift Imaging: The Basics**

- **Protons in fat** and **water** resonant at different frequencies

- Tissue containing lipid and water (spleen, kidneys, adenomas) demonstrate lower signal density on **out-of-phase** (destructive) than **in-phase** (additive) images. Mayo-Smith 2001;21:995-1012

- Chemical Shift Imaging is sensitive for differentiating adenomas from metastases. Chong et al. Radiographics 2006; 26:1811-1826
Outline

- Patient Presentation
- Differential Diagnosis
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- Menu of Radiologic Tests/Imaging Algorithm
- Diagnostic Interventions
  - Classification: What kind of adenoma is this?
    - Functioning
      - Cortex- Conn’s, Cushing’s, hyperandrogenism
      - Medulla- Pheochromocytoma
    - Nonfunctioning
      - Cysts, myelolipomas, previous trauma
- Therapeutic Interventions
Abdominal MRI T2 Fat Sat Axial cut shows Right Pheochromocytoma

Pheochromocytoma
- Large, heterogenous adrenal mass with increased signal

Atrophied contralateral adrenal

Source: Mayo-Smith W W et al. Radiographics 2001;21:995-1012
Patient 1: Lab data, PMH concerns for PA

- Our Patient’s lab results showed an elevated aldo:renin ratio. In concert with his history of hypokalemia, this concerns for primary aldosteronism.

- The gold standard for diagnosis of primary aldosteronism is Adrenal Venous Sampling.
Why Adrenal venous sampling (AVS)?

- **Gold Standard for Diagnosis of PA**
  - Nuclear Scintigraphy (NP-59) can also assesses cortical function but is expensive and results are less specific and quantitative.

- **Determines Laterality**

- **Determines Treatment Options**
Indications for and Risks of AVS

- **Indications**
  - Primary Aldosteronism
    - Adenoma vs. Hyperplasia
  - Pheochromocytoma
  - Adrenal Cushing’s

- **Contraindications**
  - General

- **Complications**
  - Adrenal Hemorrhage/venous perforation
  - Adrenal Infarction
  - Hypertensive crisis


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**AVS Procedure**

1- Planning
   - Venous Imaging via CT or MR venography

2- Vascular Access
   - Via Seldinger technique
   - Sample IVC below, above level of adrenal veins

3- Ensure entry into adrenal vein
   - Inject contrast
   - Sample adrenal veins b/l (baseline measurement)

4- Sampling
   - Inject ACTH
   - Remove samples b/l at 5min, 10min, 15min

5- Interpretation of Results
Pre-procedure Venography Identifies Adrenal Vein Anatomy

Right Adrenal Vein Variants

Source: Daunt N Radiographics 2005;25:S143-S158

Left Adrenal Vascular Supply

Source: Elsayes K M et al. Radiographics 2004;24:S73-S86
Rationale for Pre-AVS Venography

- Right Adrenal Vein
  - Can arise:
    - 1- Directly off IVC (most commonly)
    - branches at variable angles
    - 2- Branch of R renal vein
    - 3- Branch of accessory hepatic vein

- Left adrenal vein of less concern because
  - Larger size
  - Less variable anatomy
  - Arises as branch of Left renal vein


Elsevier Netteranatomy.com
Companion Patient 2: CT illustrates most common origin of R adrenal vein off IVC

Source: Daunt, N. Radiographics 2005; 25:S143-S158
After preprocedure imaging has been interpreted and incorporated into procedural planning (to reduce risk of venous perforation), we achieve access via the Seldinger technique.
AVS Procedure: Step 2

1- Planning
   - Venous Imaging via CT or MR venography

2- Vascular Access
   - Achieve vascular access via the Seldinger technique
   - Sample IVC inferior and superior to level of the adrenal veins

3- Ensure entry into adrenal vein
   - Inject contrast
   - Sample adrenals b/l (baseline measurement)

4- Sampling
   - Inject ACTH
   - Remove samples b/l at 5min, 10min, 15min

5- Interpretation of Results
Vascular Access in Adrenal Vein Sampling

- **Seldinger Technique**
  - Micropuncture
  - Femoral vein
  - Pass small guidewire
  - Pass catheter over guidewire
  - Remove wire

Cannulation of Adrenal veins Schematic

http://www.ucumberlands.edu/

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AVS Procedure: Step 3

- 1- Planning
  - Venous Imaging via CT or MR venography
- 2- Vascular Access
  - Peripheral, Femoral
  - Obtain baseline IVC samples above, below adrenal veins
- 3- Ensure entry into adrenal vein
Companion Patient 3: Fluoroscopy aids in confirmation of catheter position

Contrast injection confirms position in right adrenal vein

Source: Melby, J. NEJM 1967; 277:1050-1056

Mayo-Smith W W et al. Radiographics 2001;21:995-1012
AVS Procedure: Step 4

1- Planning

- Venous Imaging via CT or MR venography

2- Vascular Access

3- Ensure entry into adrenal vein
   - Inject contrast
   - Sample adrenals b/l (baseline measurement)

4- Sampling

- Inject ACTH
- Remove samples b/l at 5min, 10min, 15min

5- Interpretation of Results
1- Inject ACTH
2- Venous Samples collected at 5, 10, 15min

Level of renal veins

Right adrenal vein arising from tertiary R hepatic vein

T10 T11 T12

Left Adrenal Vein Sampling

Source: BIDMC, PACS Courtesy of Dr. Faintuch

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AVS Procedure: Step 5

1- Planning
   - Venous Imaging via CT or MR venography

2- Vascular Access

3- Ensure entry into adrenal vein
   - Inject contrast
   - Sample adrenals b/l (baseline measurement)

4- Sampling
   - Inject ACTH
   - Remove samples b/l at 5min, 10min, 15min

5- Interpretation of Results
   - Ensure quality samples
   - Assess laterality
Interpreting AVS Results

- **Quality**
  \[
  [\text{cortisol}]_{\text{adrenal vein}} : [\text{cortisol}]_{\text{peripheral vein}} > 2-3
  \]

- **Laterality**
  \[
  [\text{aldo}] / [\text{cortisol}]_{\text{dominant}} : [\text{aldo}] / [\text{cortisol}]_{\text{nondominant adrenal vein}} > 4
  \]

Patient 1’s AVS Results

Our patient’s results returned (as they are a send-out lab):

Left Adrenal vein produced >20 times the aldosterone made by the right adrenal gland!
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  - Medical Management
    - Familial Adrenal Hyperplasia \(\rightarrow\) glucocorticoids
    - Idiopathic b/l adrenal hyperplasia \(\rightarrow\) aldosterone receptor antagonist
  - Adrenalectomy
    - Surgical
    - CT-guided RFA
Elevated, Nonsuppressable Aldo/Plasma Renin Ratio

AVS

- Lateralization
  - Aldosterone-secreting adenoma
- No Lateralization
  - Idiopathic b/l adrenal hyperplasia

Adrenalectomy

Medical Mgmt

RFA

Surgical Adrenalectomy

Elevated ratio not suppressed by:
1. IV saline load
2. Fludrocortisone suppression test
Why Radiofrequency Ablation (RFA)?

- **Curative**
  - Adrenalectomy cures hypertension in majority of cases of Conn’s Syndrome, improves blood pressure in remainder.

- **Potential for Better Outcomes**
  - An outpatient procedure that spares more of the healthy adrenal gland and can be repeated prn.
  - CT-guided RFA promises reduced morbidity, mortality and cost compared to surgical adrenalectomy.
Indications for, Risks of RFA of Adrenal Adenomas

- Indications
  - Benign tumors
  - Small malignancies
  - Debulking procedures

- Contraindications
  - General

- Risks:
  - Bleeding, pain, infection, CVA/MI, damage to adjacent structures, death, incomplete treatment

Adrenal RFA Procedure: Step 1

1- Preprocedure Imaging
   - CT estimates position

2- Gain Access
   - Paraspinal Approach
     - Superior to rib (12th)
     - Lateral to spinous process of T12

3- Ablation
   - Deliver pulses in 5min intervals

4- Post-contrast CT
   - Retarget areas of incomplete ablation
Patient 1 CT: Classic Appearance of Adenoma

Left Lateral Decubitus C- CT Axial slice at Level of T12

Classic Adenoma CT Findings:
1- Small (<1cm)
2- Homogenous
3- Hypodense
   - <10HU (lipid-rich)
   - 20-25HU (lipid-poor)

Source: BIDMC, PACS

Patient 1 CT: Measurement estimates probe trajectory

Aorta
Adrenal Adenoma
Left Kidney
Pancreas

Source: BIDMC, PACS
Adrenal RFA Procedure: Step 2

- **1- Preprocedure Imaging**
  - CT estimates position

- **2- Gain Access**
  - **Paraspinal Approach**
    - Superior to rib (12th)
    - Lateral to spinous process of T12

- **3- Ablation**
  - Deliver pulses in 5min intervals

- **4- Post-contrast CT**
  - Retarget areas of incomplete ablation

Patient 1: CT-fluoro from RFA Procedure

Pre-ablation

- Grounding pads on chest (ground electric field)
- Local anesthesia, advance probe
- CT-fluoro allows for 3-D confirmation of probe placement (Axially, Craniocaudally)

Ablation

- 1- Begin longitudinally in deepest portion of tumor
- 2- Ablate in 5min intervals (to 60-65°C)
- 3- Reposition in new plane
- 4- Repeat until ablation cylinders overlap

Source: BIDMC, PACS

RFA Electrode: General Information

- RF electrode
  - Insulated shaft, uninsulated tip
  - Internal 200-watt generator
  - Internally cooled with perfusion pump (10°C-20°C)
    - Circulates ice water at 80mL/min
  - *if tumor >4cm, can use “cluster” RFA electrode (3 electrodes spaced 5mm apart)

Dupuy D E et al. Radiographics 2002;22:S259-S269
Adrenal RFA Procedure: Step 4

1- Preprocedure Imaging
   - CT estimates position

2- Gain Access
   - Paraspinal Approach
     - Superior to rib (12th)
     - Lateral to spinous process of T12

3- Ablation
   - Deliver pulses in 5min intervals

4- Post-ablation CT with contrast
   - Coagulation necrosis = evidence of ablation
   - Retarget areas of incomplete ablation

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Our Patient: Follow-up

- He recovered well from RFA but represented over 1 year later with increasing hypertension.
- Repeat AVS $\rightarrow$ Left aldo-secreting adenoma
- Repeat RFA $\rightarrow$ 6mm lesion was ablated
- f/u $\rightarrow$ on $\frac{1}{2}$ as many anti-hypertensive meds
Take Home Points

- **1- Refractory HTN ≠ Knee-Jerk Renal US**
  - PA = most common cause of Secondary HTN

- **2- Normal Adrenals-wispy, Y-shaped Unicorns**
  - If an incidentaloma is large, heterogenous or hyperdense (HU >20-25), consider 3-phase (delayed contrast) CT or MR shift imaging

- **3- IR’s role in the diagnosis and treatment of PA**
  - AVS → gold standard for diagnosis
  - RFA → new treatment option with proposed better outcomes
Elevated, Nonsuppressable Aldo/Plasma Renin Ratio

**AVS**
- Lateralization
  - Aldosterone-secreting adenoma
- No Lateralization
  - Idiopathic b/l adrenal hyperplasia

**Adrenalectomy**

**RFA**
- Surgical Adrenalectomy

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