Prosthetic Vascular Graft Infection

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Medical device market in USA:
- $86 billion in 2006, 10%↑for 2007

2.3 million prosthetic graft surgeries/year
- Access for hemodialysis
- Aortic aneurysm
- Vascular occlusive disease
Prosthetic Vascular Graft Surgery

- Types of graft materials
  - Autogenous vessels
  - Allograft vessels
  - Heterografts
  - Tissue engineered
- Synthetic:
  - polyethylene terephthalate (Dacron)
  - polytetrafluoroethylene (PTFE)
  - polyurethane (PU)
Failure in Synthetic Vascular Grafts

- Acute thrombosis: lack of functional endothelium

- Anastomotic site complications:
  a) Re-stenosis: foreign material induced chronic inflammatory response
  b) Aneurysm: compliance mismatch
  c) Bleeding

- Infection: foreign material
Hemodialysis (HD) Grafts

- 300,000 pts require vascular access for HD
  - 60% use synthetic grafts (180,000) due to lack of autogenous vessels for AV fistula formation
- Bacteremia in 48% - 73% patients
  - 20 to repeated puncture
- 9% - 35% of synthetic grafts become infected
  - Major source of morbidity: temporary catheter, prolonged hospitalizations
  - Substantial mortality: 12% - 36% deaths
HD Grafts

Graft infection (n=90)*
- Within 1 month of surgery: 15%
- >1 month- 12 months: 44%
- > 1 year: 41%
- Must be removed when bacteremia persist

Infection in HD Grafts

Clinical presentation

- Local signs: redness, warmth, swelling, tenderness, drainage

- No local signs
  - FUO, persistent bacteremia, ↑WBCs
  - Silent graft infection in clotted nonfunctioning grafts*
    - 62% nonfunctioning grafts in febrile patients

Diagnostic Imaging

- Scant literature available

- Ultrasound: used for imaging thrombosis/stenosis

- Labeled leukocyte imaging (WBC) for HD graft infection
# WBC Imaging

<table>
<thead>
<tr>
<th>Study</th>
<th>n=</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palestro et al* (JNM 1990)</td>
<td>30</td>
<td>100% (15/15)</td>
<td>93% (14/15)</td>
<td>97% (29/30)</td>
</tr>
<tr>
<td>Ayus &amp; Sheik-Hamad</td>
<td>41</td>
<td>100% (33/33)</td>
<td>75% (6/8)</td>
<td>95% (39/41)</td>
</tr>
</tbody>
</table>

*(Antibiotics treatment no effect on sensitivity)*
WBC Imaging

- False (+) results
  - Perigraft bleeding/ hematoma
  - Graft thrombosis

- < 1 week old post-implantation
WBC Imaging

For patients with suspected HD graft infection

- Obtain whole blood from patients day after dialysis
- Inject labeled leukocyte at another vascular site
- Image before dialysis
$^{111}$In-WBC Imaging

Forearm graft

Lt groin graft
Bypass Vascular Graft Surgery

- For aortic aneurysm and peripheral vascular occlusive disease

- 7,172 AAA elective repairs with graft: conventional and endovascular surgery
  (National Inpatient Sample Data, 2001)

- 14,788 infrainguinal bypass graft surgery
  (VA NSQIP Registry 1995-2003)
Prosthetic Vascular Graft Infection

- Risk of infection: low

- Conventional Surgery
  - First Implantation: 1-6%
    - Aortic grafts: 0.5-1.0%
    - Aorto-femoral grafts: 1.5-2.0%
    - Infrainguinal grafts: 6%
  - Revision/resection: 22%

- Endovascular aneurysm repair (EVAR): <0.4%
Prosthetic Vascular Graft Infection

**Morbidity**
- Aortic: 21%- 30% (Loss organ function)
- Peripheral: 79% (Distal limb occlusion, amputation)

**Mortality**
- Aortic: 25% -75%
  - Bacteremia/Sepsis
  - Fistula formation: hemorrhage
- Peripheral grafts: 17% - 22%
  - Bacteremia/Sepsis
Prosthetic Vascular Graft Infection

Early: \( \leq 3 \) months post-surgery
- Intraoperative/perioperative contamination
- Poor wound healing (inguinal graft sites)
- Systemic signs/symptoms present: fever, ↑ WBCs, graft dysfunction or anastomotic bleeding

Late: \( > 3 \) months
- Graft access, remote infectious site
- Can be subtle: vague discomfort, limb ischemia
- Overt: hemorrhage from aorto-enteric fistula
Diagnostic Imaging of Prosthetic Vascular Graft Infection

- Morphologic imaging
  - Sonogram: peripheral grafts
  - MRI: all grafts
  - CT: all grafts

- Functional imaging (all grafts)
  - Gallium
  - WBC
  - $^{18}F$-FDG
Morphologic Imaging

- Direct visualization of abnormalities
- Aspiration
- Fast
- Challenge

Differentiating postoperative changes from infection in grafts ≤ 3 months old
Postoperative Changes

- **Hematoma**
  - Present in all pts
  - Resolves in 7-65 days in 82% pts
  - Resolution around aortic graft faster than femoral grafts

- **Perigraft fluid**
  - Resolves over 3 months

- **Perigraft gas**
  - Resolves in 1 week

- **Fibrosis/graft incorporation**
  - Begins in 2-3 months
Ultrasonography

- Can be performed at bedside
- Adequate for inguinal/infrainguinal grafts
- Can guide aspiration
- Infected graft
  - Perigraft fluid
    - Anechoic-hypoechoic area
MRI

- Can distinguish perigraft fluid & inflammatory changes from subacute to chronic hematoma
- Cannot distinguish between infected & sterile fluid

Criteria for PVGI

- Perigraft fluid beyond 3 months of surgery
  - Sensitivity 88%, specificity 100%*
  - n= 18 pts, 16 infected, 2 uninfected
  - 2 FN: no perigraft fluid, loss of graft incorporation

*Olofsson J Vasc Surg 1988
CT

- Imaging procedure of choice for PVGI
- High spatial resolution
- Short imaging time
- Guide aspiration
CT

Criteria for PVGI
- Perigraft fluid - suspicious beyond 3rd month of surgery
- Perigraft air - after 7 weeks post-surgery
- Attenuation of surrounding tissue
- Pseudoaneurysm
- Focal bowel thickening

Aortic Grafts
- Sensitivity 94%, specificity 85%

Peripheral grafts
- Sensitivity 100%, specificity 79%
10 y/o Infected Aortobifemoral Graft

Native Aorta

Aortobifemoral Graft

Native Femoral Vessels
10 y/o Infected Aortobifemoral Graft
CT

Normal graft (2 wks post-op)
CT

Normal graft (2 wks post-op)

Normal graft (6 mos post-op)
CT

Normal graft (2 wks post-op)

Thrombosed grafts

Normal graft (6 mos post-op)
CT

Normal graft (2 wks post-op)

Normal graft (6 mos post-op)

Thrombosed grafts

Infected graft

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Radionuclide Imaging
Gallium-67

- Localizes in area of inflammation
  - Transferrin delivery to inflammation
  - Lactoferrin binding at inflammation
  - Siderophore binding at inflammation
  - Direct bacterial uptake (*S. Aureus, E.coli*)
  - Macrophage uptake (via gallium receptors)
  - Leukocyte delivery to inflammation
- Limited in diagnosing aortic graft infection due to overlying GI activity
### Gallium Imaging

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic (n=16)</td>
<td>0% (0/2)</td>
<td>93% (13/14)</td>
<td>81% (13/16)</td>
</tr>
<tr>
<td>Groin (n=24)</td>
<td>100% (5/5)</td>
<td>95% (18/19)</td>
<td>96% (23/24)</td>
</tr>
<tr>
<td>ALL (n=40)</td>
<td>71% (5/7)</td>
<td>94% (31/33)</td>
<td>90% (36/40)</td>
</tr>
</tbody>
</table>

Johnson et al, AJR 1990
## Gallium vs. CT

<table>
<thead>
<tr>
<th>Modality</th>
<th>Graft Site</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>Aortic (n=16)</td>
<td>100% (2/2)</td>
<td>57% (8/14)</td>
<td>63% (10/16)</td>
</tr>
<tr>
<td></td>
<td>Groin (n=24)</td>
<td>100% (5/5)</td>
<td>79% (15/19)</td>
<td>83% (20/24)</td>
</tr>
<tr>
<td></td>
<td>ALL (n=40)</td>
<td>100% (7/7)</td>
<td>70% (23/33)</td>
<td>75% (30/40)</td>
</tr>
<tr>
<td>Gallium</td>
<td>Aortic (n=16)</td>
<td>0% (0/2)</td>
<td>93% (13/14)</td>
<td>81% (13/16)</td>
</tr>
<tr>
<td></td>
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<td>71% (5/7)</td>
<td>94% (31/33)</td>
<td>90% (36/40)</td>
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</tbody>
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Johnson et al, AJR 1990: No statistically significant differences in sensitivity/specificity.
Infected Lt. Femoral Graft

$^{67}$Ga scan (48 hrs)
Labeled Leukocyte (WBC)


Planar $^{111}$In-WBC: Dacron infrarenal aortic graft

<table>
<thead>
<tr>
<th>Days</th>
<th>Week/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Infection (+) (n= 6)</th>
<th>(+)</th>
<th>(+)</th>
<th>(+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection (-) (n= 6)</td>
<td>(+)</td>
<td>(+)</td>
<td>(-)</td>
</tr>
</tbody>
</table>

Infection (+) (n= 6)
Infection (-) (n= 6)
Planar $^{111}$In-WBC Imaging


n= 30 patients had WBC imaging before discharge

- Normal scan (n= 14)
  - Aortic graft (n=10)
  - Aortobifemoral graft (n=4)

- Abnormal scan (n=16)
  - Peripheral grafts (n=16)
  - Inguinal wounds (n=16)
  - Decreasing activity over time
## Planar $^{111}$In-WBC Imaging

<table>
<thead>
<tr>
<th></th>
<th>Grafts</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mark (AJR, 1985)</td>
<td>n= 8 Aortic, Ao-fem grafts</td>
<td>60% (3/5)</td>
<td>100% (3/3)</td>
<td>75% (6/8)</td>
</tr>
<tr>
<td>Williamson (AJR 1986)</td>
<td>n= 30 variety of grafts</td>
<td>100% (13/13)</td>
<td>88% (15/17)</td>
<td>93% (28/30)</td>
</tr>
<tr>
<td>Brunner (J Vasc Surg 1986)</td>
<td>n= 67 variety of grafts</td>
<td>100% 14/14</td>
<td>85% (45/53)</td>
<td>88 % (59/67)</td>
</tr>
<tr>
<td>Chung (JNM 1991)</td>
<td>n= 23 variety of grafts</td>
<td>100% (10/10)</td>
<td>85% (11/13)</td>
<td>91% (21/23)</td>
</tr>
<tr>
<td>Shahidi (Ann Vasc Surg 2007)</td>
<td>n= 53 Aortic, Ao-femoral, Ao-iliac grafts</td>
<td>73% (16/22)</td>
<td>87% (27/31)</td>
<td>81% (43/53)</td>
</tr>
</tbody>
</table>
# Planar $^{99m}$Tc-WBC Imaging

<table>
<thead>
<tr>
<th></th>
<th>Grafts</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiorani (J Vasc Surg 1993)</td>
<td>37 Aortic, Ao-fem grafts</td>
<td>100% (19/19)</td>
<td>94% (17/18)</td>
<td>97% (36/37)</td>
</tr>
<tr>
<td>Krznaric (NM Commun 1994)</td>
<td>21 variety of grafts</td>
<td>53% (8/15)</td>
<td>100% (6/6)</td>
<td>67% (14/21)</td>
</tr>
<tr>
<td>Prats (JNM 1994)</td>
<td>75 variety of grafts</td>
<td>100% (20/20)</td>
<td>100% (55/55)</td>
<td>100% (75/75)</td>
</tr>
<tr>
<td>Liberatore (EJVES 1997)</td>
<td>97 Ao-femoral grafts</td>
<td>100% (61/61)</td>
<td>92% (33/36)</td>
<td>97% (94/97)</td>
</tr>
<tr>
<td>Muhammad (JPMA 2000)</td>
<td>25 Femoral grafts</td>
<td>100% (2/2)</td>
<td>61% (14/23)</td>
<td>64% (16/25)</td>
</tr>
</tbody>
</table>
Planar WBC Imaging

False (+) results
- Infectious process near the graft
- Wound infection
- Hematoma
- Pseudoaneurysm
- Thrombosed graft
- Immediate post-op period (<1 week)
$^{111}$In- WBC Imaging

Infected 2 month old Rt. Fem-pop bypass graft

Infected 2 year old Aortobifemoral graft
10 Week Old Endograft
Infection versus Post-op changes
Infected Endovascular Graft

MRI                     CT                  99mTc- AGA
# Planar WBC & Morphologic Imaging

<table>
<thead>
<tr>
<th>Modality</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>111In-WBC</td>
<td>60% (3/5)</td>
<td>100% (3/3)</td>
<td>75% (6/8)</td>
</tr>
<tr>
<td>CT</td>
<td>100% (5/5)</td>
<td>100% (3/3)</td>
<td>100% (8/8)</td>
</tr>
<tr>
<td>111In-WBC</td>
<td>100% (13/13)</td>
<td>88% (15/17)</td>
<td>93% (28/30)</td>
</tr>
<tr>
<td>CT</td>
<td>75% (6/8)</td>
<td>100% (3/3)</td>
<td>82% (9/11)</td>
</tr>
<tr>
<td>111In-WBC</td>
<td>73% (16/22)</td>
<td>87% (27/31)</td>
<td>81% (43/53)</td>
</tr>
<tr>
<td>MRI</td>
<td>68% (17/25)</td>
<td>97% (32/33)</td>
<td>84% (49/58)</td>
</tr>
</tbody>
</table>

Mark (AJR, 1985)

Williamson (AJR 1986)

Shahidi (Ann Vasc Surg 2007)
Infected 2 mo-old Rt. Femoral Graft
Infected Aortobifemoral Graft

$^{111}$In WBC
Infected Aortobifemoral Graft
## WBC-SPECT/CT

*Bar-Shalom et al, JNM 2006*

24 suspected sites $^{111}$In-WBC (Planar & SPECT) vs. $^{111}$In-WBC SPECT/CT

<table>
<thead>
<tr>
<th>Grafts (n=)</th>
<th>Modality</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 (ALL)</td>
<td>$^{111}$In-WBC</td>
<td>100% (11/11)</td>
<td>8% (1/13)</td>
<td>50% (12/24)</td>
</tr>
<tr>
<td></td>
<td>SPECT/CT</td>
<td>100% (11/11)</td>
<td>92% (12/13)</td>
<td>96% (23/24)</td>
</tr>
<tr>
<td>4 (Ao-bifem)</td>
<td>$^{111}$In-WBC</td>
<td>100% (2/2)</td>
<td>0% (0/2)</td>
<td>50% (2/4)</td>
</tr>
<tr>
<td></td>
<td>SPECT/CT</td>
<td>100% (2/2)</td>
<td>100% (2/2)</td>
<td>100% (4/4)</td>
</tr>
<tr>
<td>20 (Peripheral)</td>
<td>$^{111}$In-WBC</td>
<td>100% (9/9)</td>
<td>9% (1/11)</td>
<td>50% (10/20)</td>
</tr>
<tr>
<td></td>
<td>SPECT/CT</td>
<td>100% (9/9)</td>
<td>91% (10/11)</td>
<td>95% (19/20)</td>
</tr>
</tbody>
</table>
54 y/o male, 2 y/o left femoropopliteal bypass and 2 month-old right femoropopliteal bypass grafts, presented with infected surgical wound in the right groin.

Surgical wound improved with systemic Abx and local Tx. No evidence of graft infection at 10-month follow-up
Effect of Antibiotics on WBC Imaging

- Chung et al. JNM 1991: No effect on sensitivity of WBC imaging
  - Sensitivity: 100% (10/10), Specificity 85% (11/13), Accuracy 91% (21/23)
Effect of Antibiotics on WBC Imaging

Nov 2001  Dec 2001  Jan 2002
### 18F-FDG-PET

<table>
<thead>
<tr>
<th>Grafts</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stumpe (Eur JNM 2000)</td>
<td>100% (2/2)</td>
<td>100% (5/5)</td>
<td>100% (7/7)</td>
</tr>
<tr>
<td>6 Aortic, 1 Inguinal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fukuchi (J Vasc Surg 2005)</td>
<td>91% (10/11)</td>
<td>64% (14/22)</td>
<td>73% (24/33)</td>
</tr>
<tr>
<td>33 Aortic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lauwers (Agiology 2008)</td>
<td>100% (3/3)</td>
<td>33% (2/6)</td>
<td>56% (5/9)</td>
</tr>
<tr>
<td>2 Aortobifem, 7 Peripheral</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
$^{18}$F-FDG PET

- False (+) results
  - Grafts $\leq 2$ months old
  - Healing grafts
# $^{18}$F-FDG-PET vs. CT

<table>
<thead>
<tr>
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<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fukuchi</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(J Vasc Surg 2005)</td>
<td>CT</td>
<td>64% (7/11)</td>
<td>86% (19/22)</td>
</tr>
<tr>
<td></td>
<td>FDG-PET</td>
<td>91% (10/11)</td>
<td>64% (14/22)</td>
</tr>
<tr>
<td><strong>Lauwers</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Angiology 2008)</td>
<td>CT</td>
<td>33% (1/3)</td>
<td>50% (1/2)</td>
</tr>
<tr>
<td></td>
<td>FDG-PET</td>
<td>100% (3/3)</td>
<td>33% (2/6)</td>
</tr>
</tbody>
</table>
18F-FDG-PET/CT

Keidar et al., JNM 2007

39 pts with suspected graft infection

69 total grafts imaged: 40 suspected, 29 not suspected of infection.

- Aortobifem (n= 20)
- Femoropopliteal (n= 31)
- Other (n= 18)

Age, type, site of graft provided
18F-FDG-PET/CT

- False (+) results due to infected hematoma
- Accurately identified nearby soft tissue infection
- No evidence of infection in normal 18F-FDG-PET/CT
- High negative predictive value

<table>
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<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keidar (JNM 2007)</td>
<td>n= 39</td>
<td>93% (14/15)</td>
<td>92% (22/24)</td>
</tr>
<tr>
<td>n= 18 (≤ 3 months old)</td>
<td>83% (5/6)</td>
<td>83% (10/12)</td>
<td>83% (15/18)</td>
</tr>
</tbody>
</table>
Surgical Wound Infection

68 y/o pt, left femoropopliteal bypass graft placed 18 months previously, presented with fever & infected wound in the left thigh medially.

(Keidar et al. JNM 2007)
Infected Prosthetic Vascular Graft

65 y/o patient, multiple prosthetic bypass graft surgeries, presented with fever & right thigh pain and swelling.

Courtesy: Zohar Keidar MD. PhD.
Deputy Director
Department of Nuclear Medicine
Rambam Health Care Campus
Haifa, Israel
Asymptomatic Aortic Graft

Sept 2006
SUV Max: 8.4

July 2007
SUV Max: 15.2
Prosthetic Vascular Graft Infection

- CT is the imaging procedure of choice
  - Useful for patients with grafts > 3 months old
- WBC imaging complementary to CT
  - Especially for grafts < 3 months old
- $^{18}$F-FDG PET & PET/CT
  - Initial results encouraging
  - Further investigations needed