Our Approach to the Treat To Target Paradigm in the Management of Patients with Rheumatoid Arthritis: The First Step towards Population Management

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What Is the Target for the Management of RA?

Disease activity is at the basis of the sequence of outcomes:

- Inflammation (Disease activity)
- Joint Damage
- Disability
- Impaired Quality of Life
- Costs

Disease activity should be the primary target for treatment of RA.
Overall Approach to RA Evaluation and Management

- Early diagnosis - damage can occur early
  - 2010 RA classification criteria
- Measuring RA disease activity
  - Quantitatively establish and document a baseline
  - Compare quantitative RA measurements at progressive time points
- Treatment strategy to continuously strive to push the disease toward improvement, i.e., low disease activity or remission
  - Advance therapy in stepwise fashion while continuously measuring the disease to achieve goal, or as close as is reasonably feasible.
Treat-to-Target Treatment Algorithm

Main Target:
Active RA
- Adapt therapy according to disease activity
- Use a composite measure of disease activity every 1-3 months

Alternative Target:
- Adapt therapy according to disease activity

CLINICAL
- MD-HAQ/RAPID-3
- Physician GLOBAL
- SWOLLEN JOINT COUNT
TRUST CLINICAL MEASURES
BUT
VERIFY WITH LAB AND IMAGING MEASURES

- CLINICAL
  - MD-HAQ/RAPID-3
  - Physician GLOBAL
  - SWOLLEN JOINT COUNT
INFLAMMATORY ARTHRITIS DISEASE ACTIVITY ASSESSMENT FACTS

COMPREHENSIVE EVALUATION OF PATIENT’S STATUS

- **CLINICAL**
  - MD-HAQ/RAPID-3
  - Physician GLOBAL
  - SWOLLEN JOINT COUNT

- **LABORATORY**
  - Vectra DA

- **IMAGING**
  - ULTRASOUND PROFILE
Vectra® DA:
The multi-biomarker blood test that gives you a deeper look at RA disease activity
CLINICAL
- MD-HAQ/RAPID-3
- Physician GLOBAL
- SWOLLEN JOINT COUNT

LABORATORY
- Vectra DA

IMAGING
- ULTRASOUND PROFILE
Objective Measures of RA Disease Activity

- **Vectra DA** is a multibiomarker test with components representing tender and swollen joints and patient global health.
- **Ultrasound** score also contains components associated with tender, swollen joints.
- **Rapid-3** contains info on pain, function and patient global health.

The three measures, Vectra DA, Rapid-3 and Ultrasound should be complementary in predicting disease severity and managing disease activity to prevent erosions.
Inflammatory Arthritis Ultrasound Profile (IAUP)

- Standardized US tech-performed dorsal scan of 4 MCPs, 4 MTPs, and both wrists/ECUs. Use 16MHz matrix array probe on GE Logic 9. Scans uploaded to cloud for remote analysis.
- Performed as part of clinical visit or by separate appt.
- Score on semi-quantitative scale 0-3 for each component.
- 12 points possible per joint/24 points possible per component/96 total points possible.
- Quantitative measurement of synovial thickness in MCPs and blood flow in Power doppler + tissue.

Rapid-3 recorded by US tech at same time as IAUP.
**Inflammatory Arthritis Ultrasound Profile (IAUP)**

**Clinical Utilization**

**Targets to Measure/Follow**
- Total points
- Total synovial thickness
  - Normal < 2.0
- Individual component scores
  - Power Doppler Peak Pixel Density
- Signal joint(s) score

**Qualitative**
- Symmetrical v asymmetrical
- Relationship to Rapid-3

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**INFLAMMATORY ARTHRITIS ULTRASOUND PROFILE™**

<table>
<thead>
<tr>
<th>Patient Name</th>
<th>Date</th>
<th>PD</th>
<th>ER</th>
<th>EF</th>
<th>SY</th>
<th>Total</th>
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**Diagnosis**

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**Sonographer**

<table>
<thead>
<tr>
<th>Date</th>
<th>MDHAQ Rapid 3</th>
<th>TST</th>
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**Date of Scan**

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<tr>
<th>Hand</th>
<th>Last X-ray:</th>
<th>Foot:</th>
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**WRIST**

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<th>PD</th>
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**ECU**

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**HAND**

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<tr>
<th>MCP</th>
<th>Power Doppler (PD)</th>
<th>Erosion (ER)</th>
<th>Effusion (EF)</th>
<th>Synovium (SY)</th>
<th>MCP Synovial Thickness (cm)</th>
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**FOOT**

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<th>MTP</th>
<th>Power Doppler (PD)</th>
<th>Erosion (ER)</th>
<th>Effusion (EF)</th>
<th>Synovium (SY)</th>
<th>MCP Synovial Thickness (cm)</th>
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**Sonographer Comments:**

- Rapid-3 recorded at same time.
Inflammatory Arthritis Ultrasound Profile (IAUP) Clinical Utilization

Establish diagnosis of early RA by detecting synovitis (synovial thickness/effusion, power doppler +) &/or erosions.

Assess prognosis for erosive disease (Power doppler +, ECU abnormalities)

Early detection of erosive disease compared to x-ray.

Differentiate active from inactive erosion. (power doppler + or -)

Allows determination of disease severity at onset and improvement/deterioration of individual component or total in response to therapy.
Inflammatory Arthritis Ultrasound Profile (IAUP) Clinical Utilization

Frequency of Performing IAUP

Active disease with monthly treatment visits to adjust meds to achieve remission/low disease activity - Q 3 months

Sustained low disease activity as measured by SJC, MD global, Rapid-3 and Vectra DA- Q 6 months

Sustained Remission as determined by SJC, MD global and Vectra DA- Q 12 months.

Rapid-3 recorded at same time.
Bone Erosion

- An intraarticular discontinuity of the bone surface that is visible in 2 perpendicular planes.
Ultrasound Imaging in Rheumatoid Arthritis
3rd MC Head Erosion

transverse

longitudinal
Measurement of Bone Erosion

longitudinal

transverse
Ultrasound Imaging in Rheumatoid Arthritis
3rd MC Head Erosion
Dynamic Scanning
Power Doppler
Grade 3
R Wrist
Gr3 Power Doppler
Peak Pixel Density
Ultrasound Imaging with Power Doppler in Rheumatoid Arthritis
A TALE OF TWO MCPs

Initial Visit

TST=0.72
TST=0.70

Measure both grey scale and power doppler as evidence of synovitis
Study both hands and feet not only the dominant side or the most painful
While erosions can be seen on MRI there is no way to tell if they are active or inactive.
Objective Measures of RA Disease Activity

- Provide targets to treat towards
- Facilitate discussions with patients
- Help to select and monitor most efficacious therapies
- Help to decide when/if to taper medications
Objective Measures of RA Disease Activity

- **Vectra DA** is a more sensitive measure of RA disease activity than the ESR and CRP.
- Elevated values for Vectra DA highly predictive of development of erosive disease.
- **Ultrasound** is more sensitive than x-ray for the detection of erosions. Erosions are the worst prognostic factor.
- Power doppler positive and grey scale synovitis are highly-predictive of erosive disease.
Objective Measures of RA Disease Activity

High likelihood of erosive disease

Vectra DA = 75 + Power Doppler = Grade 3

No medications have been added
Objective Measures of RA Disease Activity

• Provide targets to treat towards
• Facilitate discussions with patients
• Help to select and monitor most efficacious therapies
• Help to decide when/if to taper medications
SWEFOT Vectra® DA Analysis Overview

- Patients from 15 rheumatology units in Sweden
- Early rheumatoid arthritis (eRA) patients with disease duration <1 year, DMARD naïve

X-ray #1 → ΔSHS → X-ray #2
Clinical Data

Vectra DA (N = 235)
Assess Response

BL month 3 year 1
Start MTX

R → MTX
NR → MTX/H/S, MTX/Inf

ΔR = Responders
NR = Non Responders
MTX/H/S = Methotrexate with sulfasalazine and hydroxychloroquine
MTX/Inf = Methotrexate with infliximab

Objective Measures of RA Disease Activity

- Vectra DA is often elevated prior to the development of erosive disease.
- Early RA - elevated vectra DA with no erosions, +/- PD+ or grey scale synovitis.

Vectra DA= 39; Rapid3=15
Pt AK
Sxs for 2 mos, Rapid 3 = 15.3, SJC=0
RF/CCP strong+, +Family Hx

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**Parameter** | **Value** | **m1** | **m2** | **m3** | **m4** | **m5** | **m6** | **Method**
--- | --- | --- | --- | --- | --- | --- | --- | ---
PD | ER | EF | SY | MCP 5/48 | MTP 0/48
R2MCP | 0 | 0 | 0 | 1 | **GAIN 12.5** | 12.5
R3MCP | 0 | 0 | 0 | 1 | **TST 2.09**
L2MCP | 0 | 0 | 1 | 1 | **RAPID 3: 15.3**
L3MCP | 0 | 0 | 0 | 1 | BLT ECU PD 0, EF 0
R5MTP | 0 | 0 | 0 | 0 | LT ECU DISPLACED
R2MTP | 0 | 0 | 0 | 0
L5MTP | 0 | 0 | 0 | 0
L2MTP | 0 | 0 | 0 | 0
TOTAL | 0 | 0 | 1 | 4 | **5/96**

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Begin Mtx tabs 20 mg weekly on 5/14
Rapid3 = 4 on 8/28
Objective Measures of RA Disease Activity

- Ultrasound has defined a new type of erosion...the active erosion.
- Manifest as a power doppler + erosion
While erosions may not heal..., a target of treatment is to change an active erosion to an inactive erosion.

Pt CN

August, 2011

scMtx 25 mg/wk

August 2012

Sc Mtx 25 mg/wk
Enbrel 50 mg/wk
Objective Measures of RA Disease Activity

- Provide targets to treat towards
- Facilitate discussions with patients
- Help to select and monitor most efficacious therapies
- Help to decide when/if to taper medications
Pt resisted therapy while caring for his wife with RA of even longer duration.

She passed from complications of therapy.

Pt was begun on Mtx 4/12 with definite benefit but persistent pain.

Qgold + for Tb so required treatment before anti-tnf.

12/7 added Cimzia
RF/CCP strong +
>10 yr Hx of active disease
Treatment of active erosion

10 27 2012
Vectra DA = 64

3 14 2013
Vectra DA = 32
RF/CCP strong +  
>10 yr Hx of active disease  
Treatment of active erosion

While the R 2nd mcp is now PD-, the 3rd mcp is +, also with moderate Vectra DA. Pt’s Mtx increased to 25 mg weekly. 4 months later Rt 3rd mcp was PD- and Vectra DA= 28.
Summary

• For patients with RA, it is possible and desirable to objectively measure disease activity from multiple aspects and treat to target.

• Patient preference will largely dictate treatment progression but this can be influenced by objective data.

• Vectra DA, a multiple component bioassay, offers a biologic measure of RA disease activity.

• An Ultrasound profile of important components of RA inflammation and joint destruction offers an imaging measure of RA disease activity and severity.
Conclusion

- No one, single measure will suffice to fully describe disease activity in patients with RA.
- A Synthesis of clinical measures of patient and physician assessments of disease activity complemented by laboratory and imaging measurements will be necessary to give the full picture of disease activity and severity.
- Future treatment decisions based on this synthesis of objective measures will give the best outcomes over time for patients with RA.
NEXT STEPS
Population Management for Rheumatoid Arthritis

• Enroll all RA patients into OUR registry cataloguing objective measures, ie IAUP, Vectra DA, Rapid-3, Physician global, swollen joint count.

• Stratify patients as high, medium or low disease activity.

• Focus initially on the timely assessment of high disease activity patients (minimum Q 3 months).

• Re-design practice workflow, including pre-visit assessment.
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