

Do you like what you see? - Understanding data in magnetic resonance imaging studies

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DeOnna, living with rheumatoid arthritis



Inspired by **patients.**
Driven by **science.**

Agenda

- | **How MRI is used in Rheumatoid Arthritis (RA)**
- | **Dynamic Contrast Enhanced MRI (DCE-MRI)**
- | **Workflow in a DCE-MRI study**
- | **Data Challenges**
- | **What to consider in Protocol/SAP/other documentation**
- | **Conclusion**

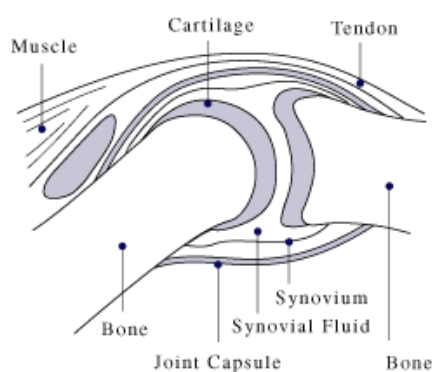


How MRI is used in Rheumatoid Arthritis?

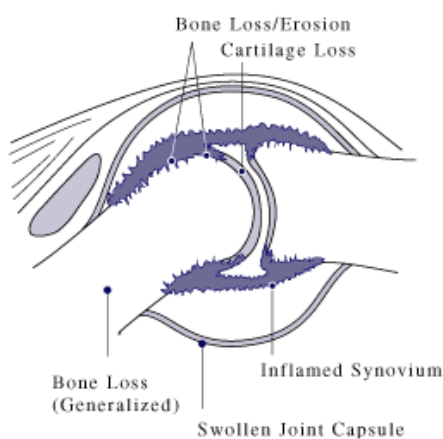
MRI can visualise soft tissues which cannot be seen in X-rays.

- Higher contrast
- Several planes

Normal Joint



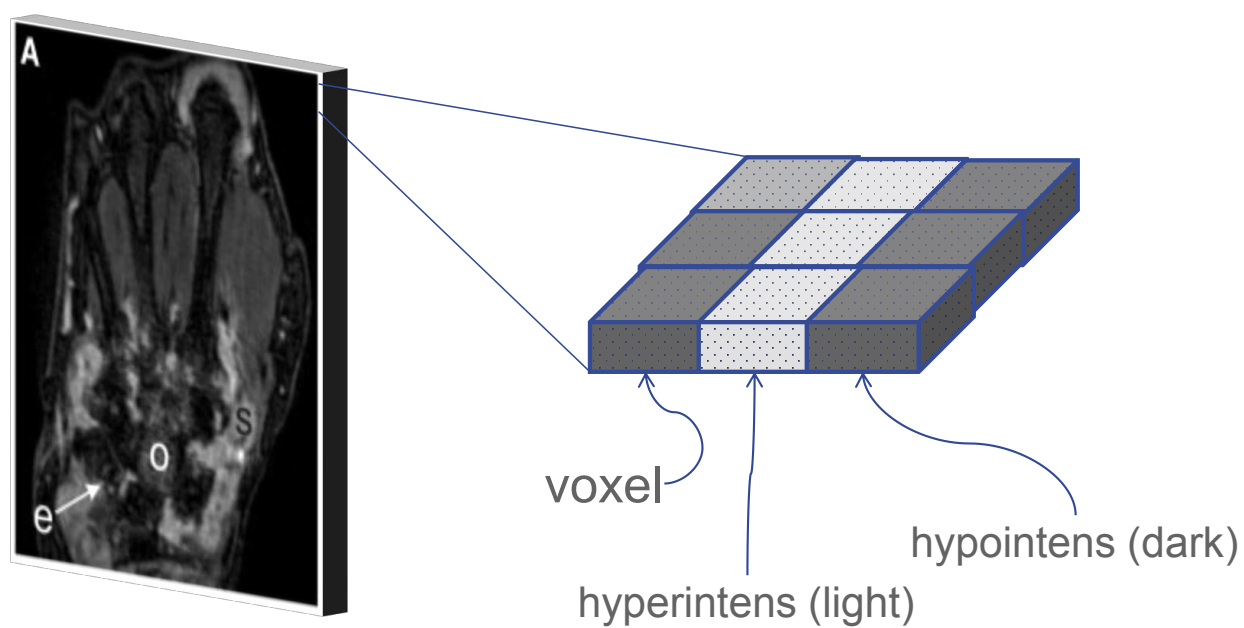
Joint Affected by Rheumatoid Arthritis



MRI shows structures not visible in X-ray e.g. edema, inflammation in soft tissues, bone erosion



MRI image (slice) is made up of voxels (volume pixels)



Dynamic contrast enhanced MRI (DCE-MRI)

Sequential images during and after administration of contrast agent

Enhancement is more intense in inflamed tissues

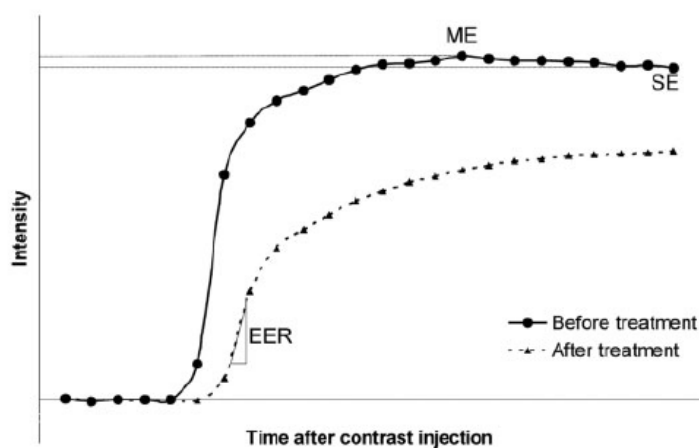
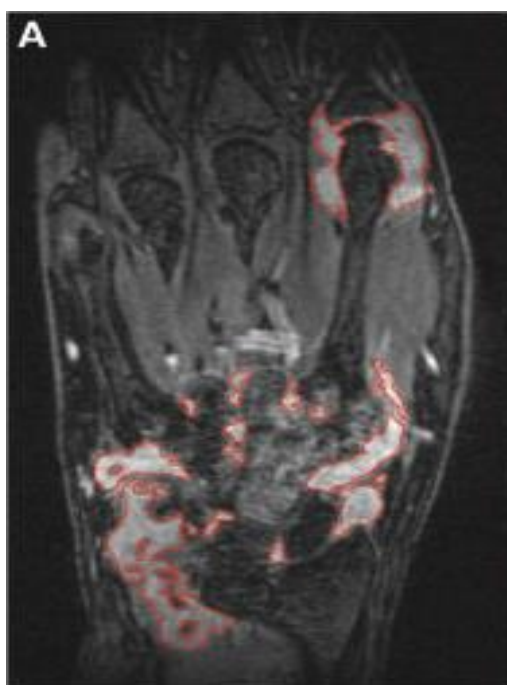


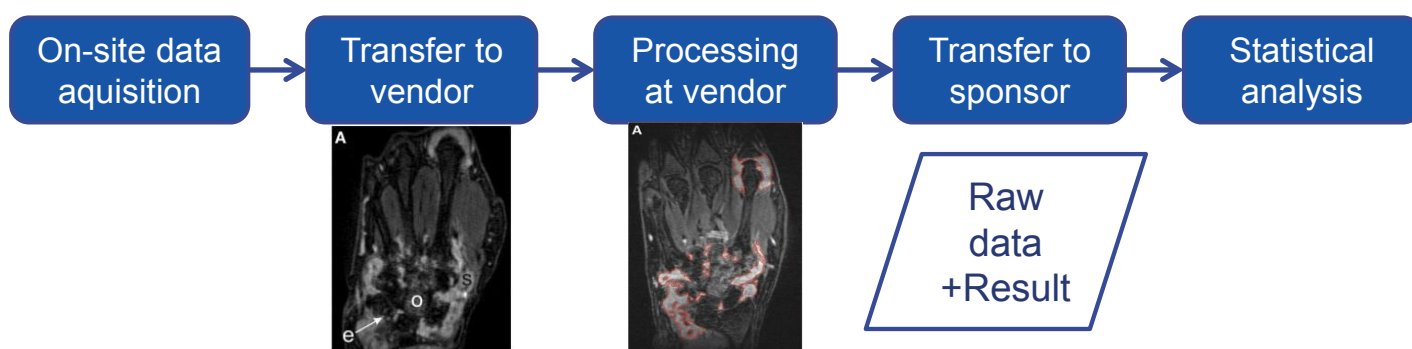
FIG. 3. Enhancement curves from a series of DCE-MRI images of a patient with RA showing the early enhancement rate (EER), the maximum enhancement (ME) and the late (static) enhancement (SE). Enhancement is reduced after anti-TNF- α therapy.

DCE-MRI

Regions of interest (manually) marked in red



Workflow in a DCE-MRI study



- **New diagnostic methods**
- **Involvement of external vendors**
- **Need to rely on documentation from vendor**

Documentation provided by vendor

Computation of results

Data transfer specifications



Computation of results

Maximum Enhancement

- E.g. in MCP 2-5

$$ME^{MCP2-5,precise} = \frac{\sum_{j=2}^5 M^{MCPj,precise} * (N_{plateau}^{MCPj,precise} + N_{washout}^{MCPj,precise})}{N_{vox}^{MCP2-5,precise}}$$

Explanation of abbreviations:

M – Mean Maximum Enhancement (ME) in the "volume" ROI

j – Joint number

N_{plateau} – Number of voxels with plateau pattern of enhancement in the "volume" ROI

N_{washout} – Number of voxels with wash-out pattern of enhancement in the "volume" ROI

MCP – MCP joints

Blinded Results from DCE-MRI

Visit	Mean ME	Std. Dev. ME	N-plateau	N-washout	N- plateau + N-washout	ME	Reader comments
Baseline	.	.	.	.	.	.	.
Visit 1	.	.	.	.	.	.	.
Visit 2	.	.	.	.	.	.	.
Visit 7	.	.	.	.	.	.	.
Baseline	.	.	.	.	.	.	.
Visit 1	.	.	.	.	.	.	.
Visit 2	.	.	.	.	.	.	.
Visit 7	.	.	.	.	.	.	.
Baseline	.	.	.	.	.	.	.
Visit 1	.	.	.	.	.	.	.
Visit 2	.	.	.	.	.	.	.
Visit 7	.	.	.	.	.	.	.



Test Dataset of Results from DCE-MRI

Visit	Mean ME	Std. Dev. ME	N-plateau	N-washout	N- plateau + N-washout	ME	Reader comments
$ME^{MCP2-5,precise} = \frac{\sum_{j=2}^5 M^{MCPj,precise} * (N_{plateau}^{MCPj,precise} + N_{washout}^{MCPj,precise})}{N_{vox}^{MCP2-5,precise}}$							
Baseline	1,59	0,23	531	85	616	979	
Visit 1	1,46	0,16	376	103	479	701	
Visit 2	1,43	0,09	39	23	62	88	
Visit 7	1,47	0,13	31	4	35	52	
Baseline	1,79	0,19	10	65	75	134	
Visit 1	2,06	0,39	10	56	66	136	
Visit 2	2,00	0,24	10	51	56	112	
Visit 7	2,14	0,36	9	61	70	150	

Final Transfer of Results from DCE-MRI

Visit	Mean ME	Std. Dev. ME	N-plateau	N-washout	N- plateau + N-washout	ME	Reader comments
Baseline	1.59	0,23	609	185	794	1262	
Visit 1	0	0	0	0	0	0	
$ME^{MCP2-5,precise} = \frac{\sum_{j=2}^5 M^{MCPj,precise} * (N_{plateau}^{MCPj,precise} + N_{washout}^{MCPj,precise})}{N_{vox}^{MCP2-5,precise}}$							
Baseline	1,59	0,23	531	85	616	979	
Visit 1	1,46	0,16	376	103	479	701	
Visit 2	1,46	0,16	376	103	479	701	Image not readable
Visit 7	1,47	0,13	31	4	35	52	
Baseline	1,79	0,19	10	65	75	134	
Visit 1	2,06	0,39	10	56	66	136	
Visit 2	2,00	0,24	10	51	56	112	
Visit 7	2,14	0,36	9	61	70	150	

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LOCF

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Challenges for Programming

| Data Quality depends on vendor

| Completeness and consistency of data deliverables needs to be checked by statistical programming

| > 60 variables in data transfer

| Difficult to link variable names to derivations

| Challenging to re-create results

| No normal ranges, ranges of results depend on MRI technique used

| Missing data handling and imputations rules (if any)

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Proper documentation needed

Documentation

MRI procedures should be mentioned in the protocol

- Schedule of reading procedure (batch vs. ongoing read)

Details on MR image acquisition are usually provided in a separate imaging charter

- Reference document for investigators
- Image acquisition protocol (methods, schedule, shipment)
- Dataflow from sites to reader
- Reader procedure (1st, 2nd (3rd) read)

Details on MRI data deliverables are provided in a data transfer document



Data transfer document

Should cover

- Missing data algorithms
- Imputation algorithms (if any)
- Description of derived variables
- Link names of derived variables to derivations
- Should provide all information necessary to reproduce derivations

Should be seen as part of the protocol or statistical analysis plan

Statistician needs to review technical documents to be sure all variables needed are available

Dummy dataset should be available for pre-programming

- including dummy results, if trial is blinded
- Keep in mind these are idealised data

Conclusion

- | **DCE-MRI is a sophisticated method to analyse MRI data**
- | **Methodology not easy to understand without basic knowledge about MRI and related technical terms**
- | **Data quality activities are moved to statistical programmers**
- | **Documentation should enable programmers to reproduce results**
- | **Statistical programmers need to be involved much earlier in the study process to ensure all tools needed are available**

Questions?

Thanks!

