





Methodology of  
DWI MRI Lesion Volume  
Measurements and Statistical  
Implications

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# Outline

1. Background
2. Objective
3. Methods
4. Results
5. Conclusions



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# Background

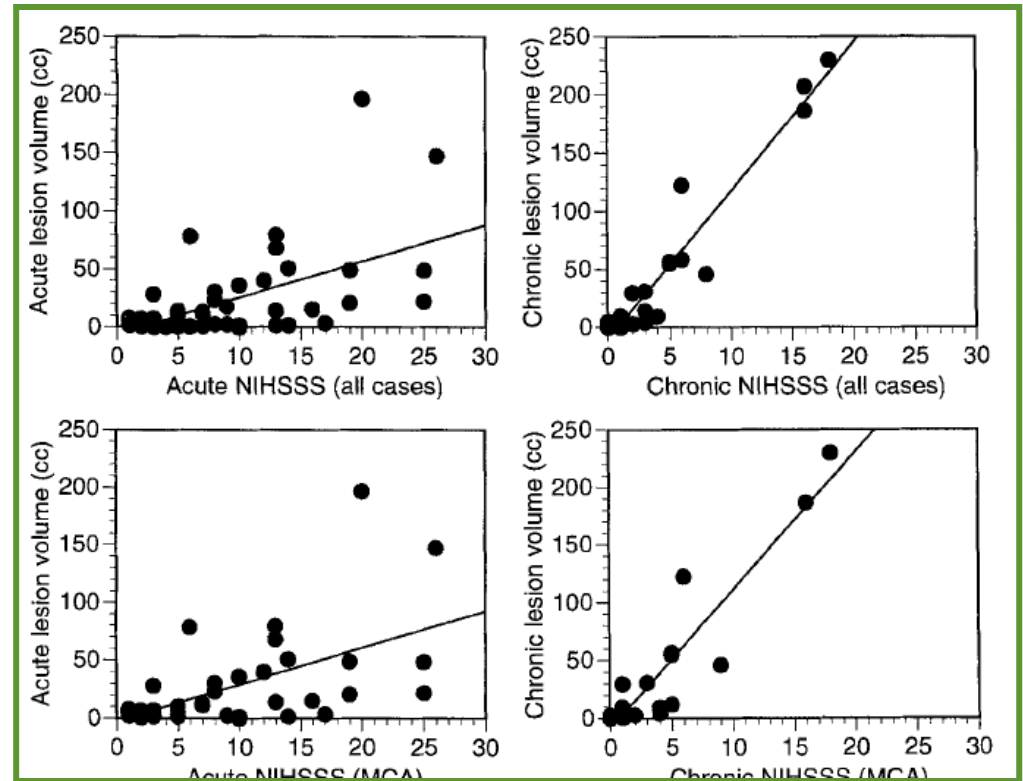
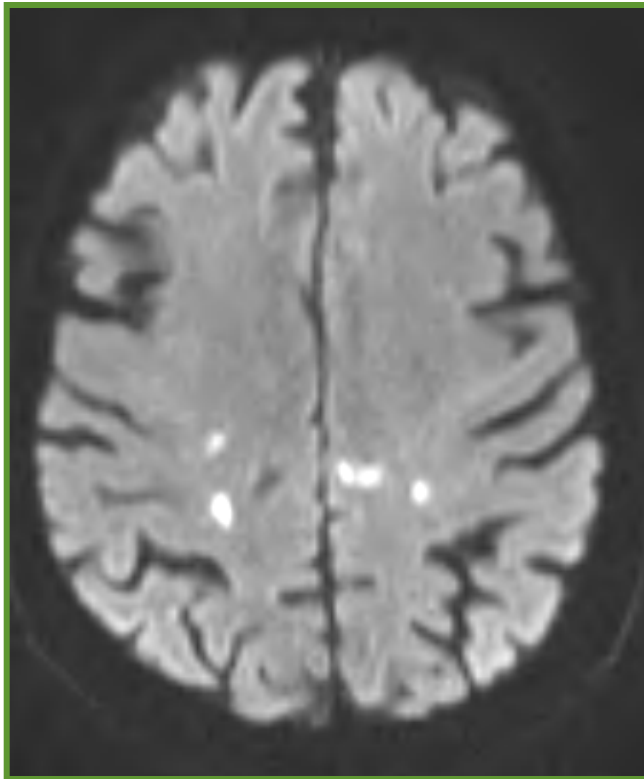


- TAVR procedures are associated with embolization of aortic and aortic valve debris and cause cerebral ischemic lesions
- Post-procedural cerebral ischemic events are associated with worse cognitive and overall outcomes
- Diffusion-weighted MR imaging of the brain is highly sensitive and specific for the detection of new cerebral ischemic lesions
- There are several different potential methods, but no accepted standards for the quantification of cerebral DWI lesions on MRI; the reproducibility of the different methods is unknown

# Background

## Acute Ischemic Lesions on DW-MRI and Cognitive Outcomes

DW-MRI is excellent for volume of acute cerebral ischemic lesions  
Imaging of acute cerebral DW-MRI is associated with worse cognitive outcomes  
ischemic lesions outcomes



# Background

## Quantification of DW-MRI Lesions



### 1. Manual 2D methods (eg. ABC/2 method)

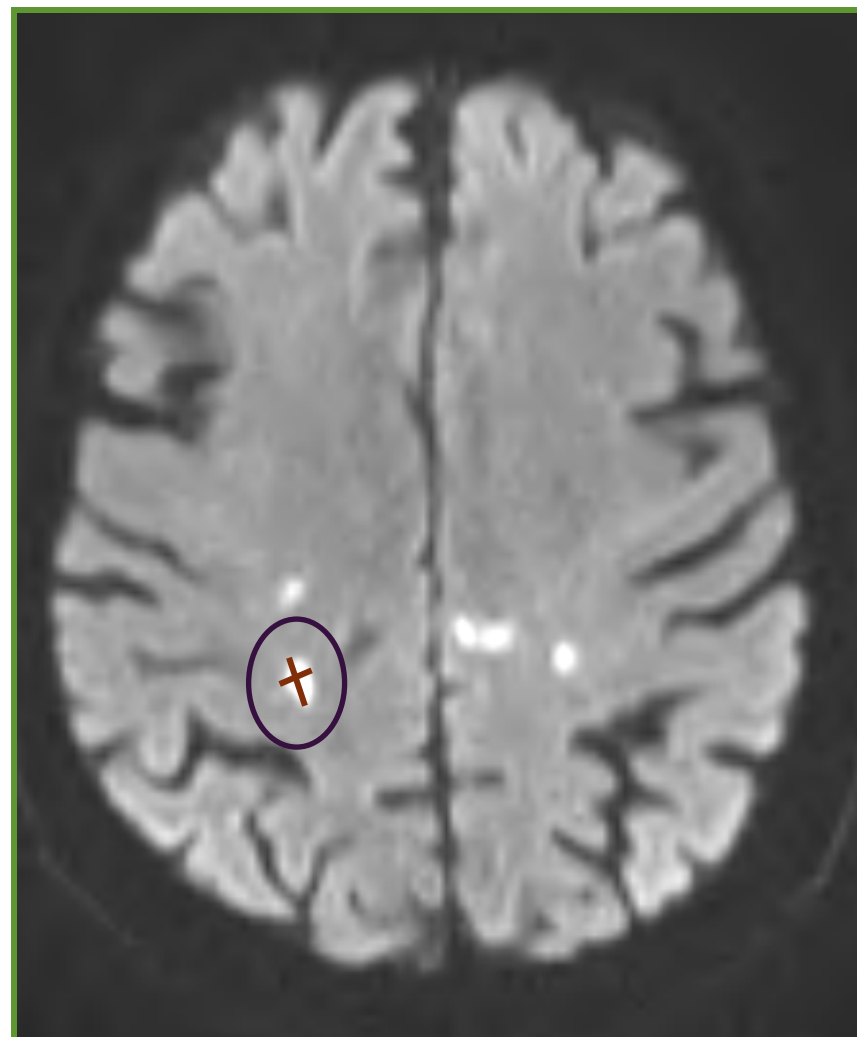
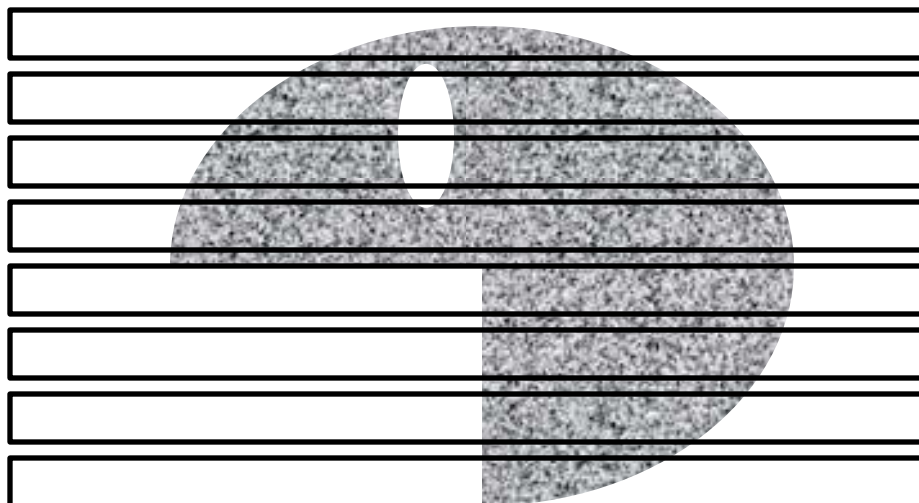
1. Manually measure diameters or area of lesions in a single, 2D slice
2. Assume the size of lesion in the third dimension based on slice thickness
3. Calculate the volume of each lesion from the measurements above

### 2. Automated 3D methods

1. Manual component is to identify lesions manually
2. Automated image segmentation software tracks each lesion based on voxel brightness in 3D

# Background

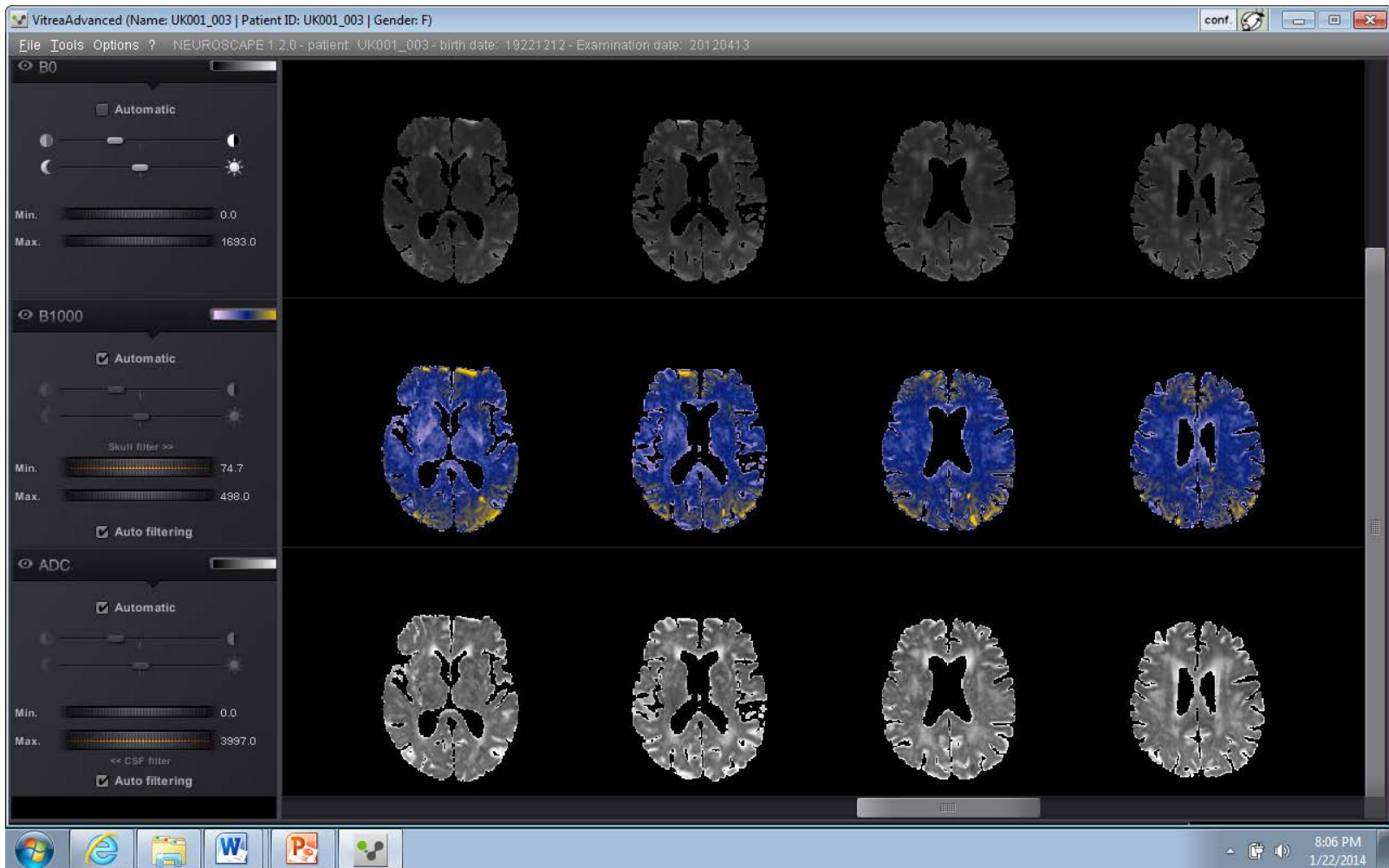
## 2D Methods





# Background

## 3D Method



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# Objective



...currently, there is no generally accepted reference standard methodology for the quantitative, volumetric assessment of DWI lesions on cerebral MR images...

...accordingly, the objective of the current project was to compare several different methodologies for the quantitative, volumetric measurements of DWI lesions, and determine and compare the overall reproducibility of the different methods...

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# Methods

## General Study Design



- Reproducibility method study was performed in the DEFLECT I clinical study
  - Enrollment criteria as per the DEFLECT I clinical study
  - MR acquisition parameters as per the DEFLECT I clinical study
- Twenty patients (n=20) with paired pre- and post-procedural image sets were evaluated
- Each image set was evaluated twice, in a blinded fashion and in random order, by two independent blinded observers
  - 2D measurements: long and short axis diameter of each lesion

# Methods

## MR Image Acquisition



Several different methods were evaluated:

- Method 1: 3D measurements
- Method 2: 2D measurements; z-axis assumed based on the largest 2D measurement
- Method 3: 2D measurements; z-axis assumed based on slice thickness and inter-slice gap

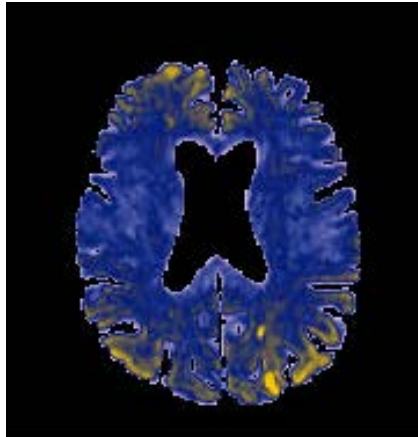
# Methods

## Image Analysis: Method 1 (3D Method)

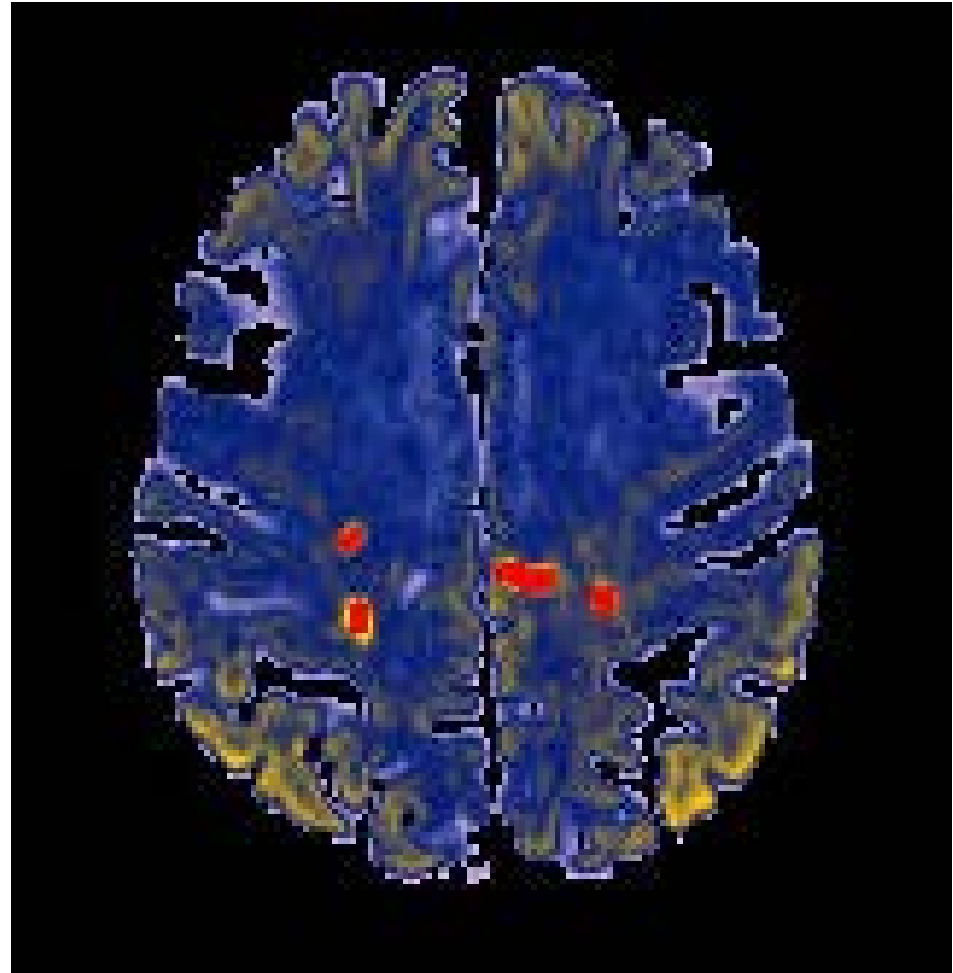
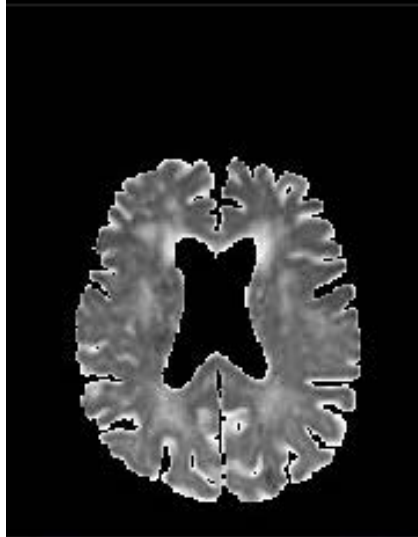


### Method 1: 3D Method

DW-MRI

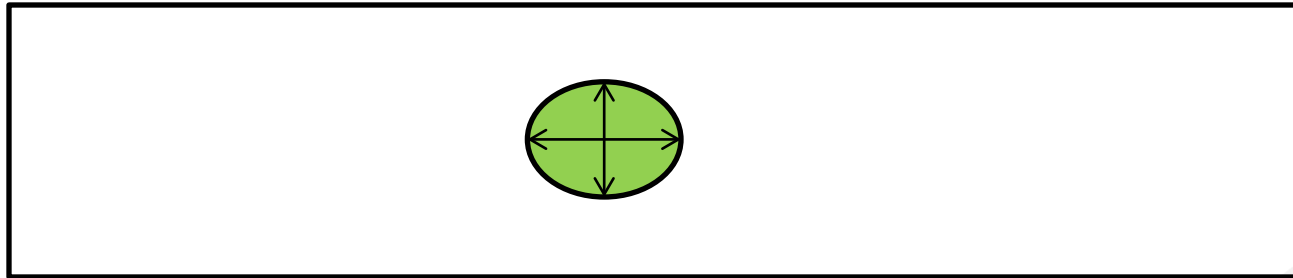


ADC



# Methods

Image Analysis: Method 1 and 2 (2D Method)



Slice  
Thickness



Slice  
Thickness

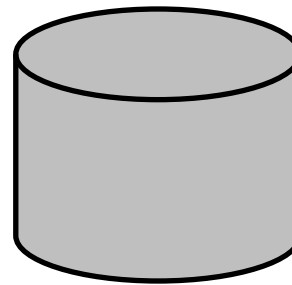
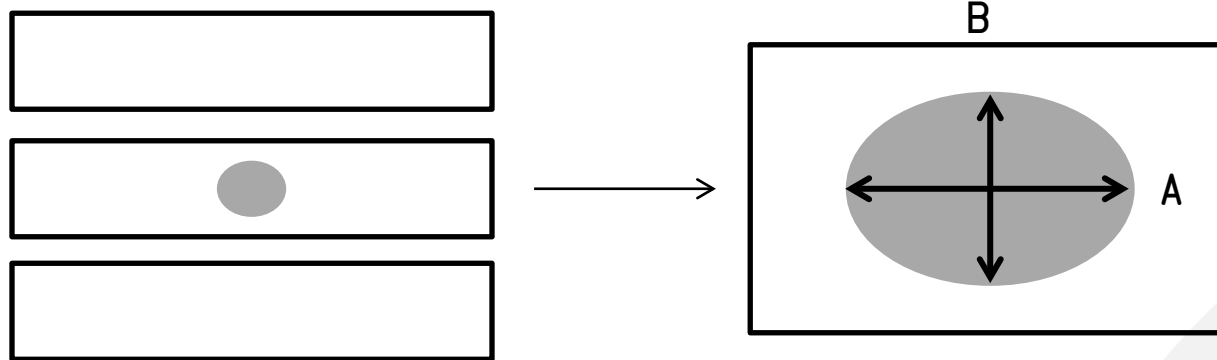
Method 2

Method 3

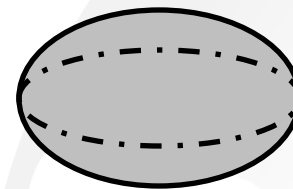


# Methods

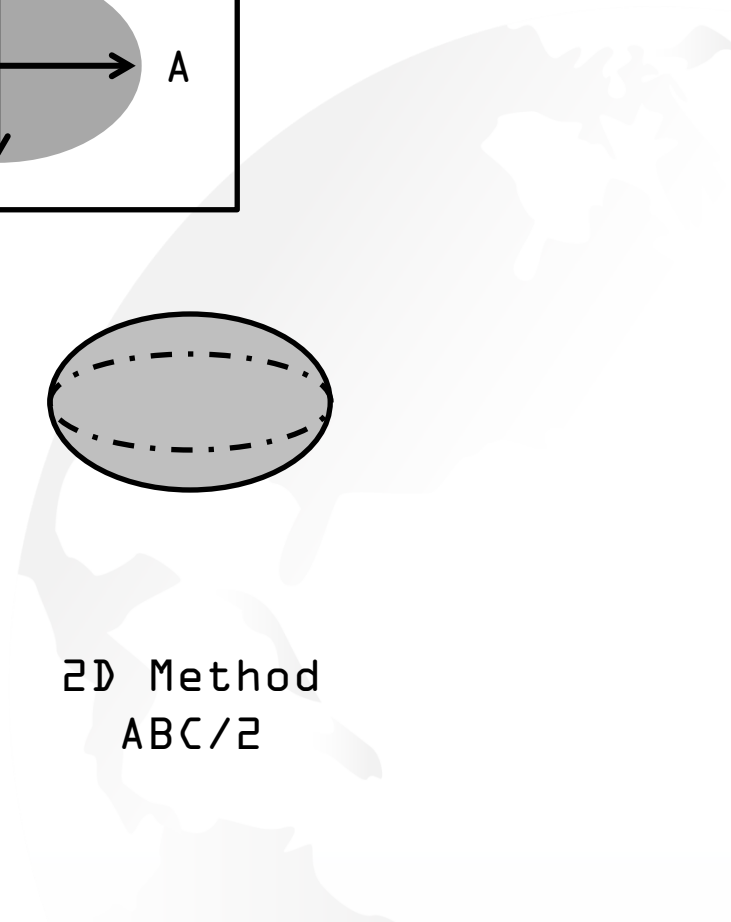
## Image Analysis: Method 4 (2D Method)



3D Method



2D Method  
 $ABC/2$



# Methods

## Statistical Analysis



- Evaluated the following:
  - Intra-rater agreement
  - Inter-rater agreement
- For the following parameters:
  - Total lesion volume
  - Average single lesion volume (not presented today)
  - Lesion number
  - Maximum lesion volume (not presented today)
- Using the following metrics:
  - Correlation concordance coefficient
  - Mean difference and limits of agreement (LOA) based on Bland-Altman analysis

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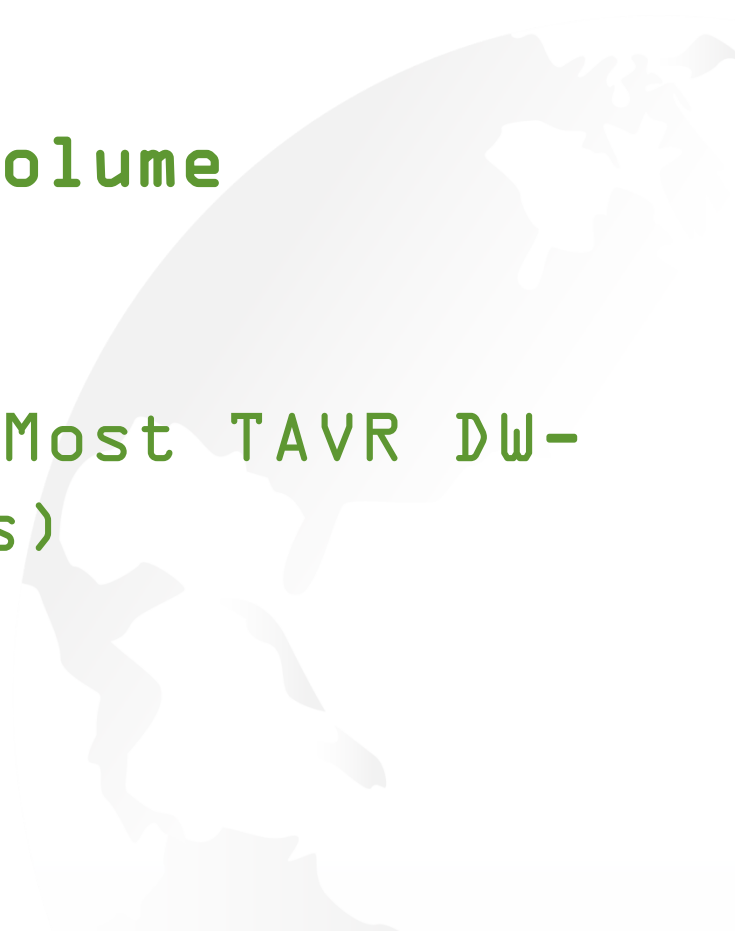


# Results



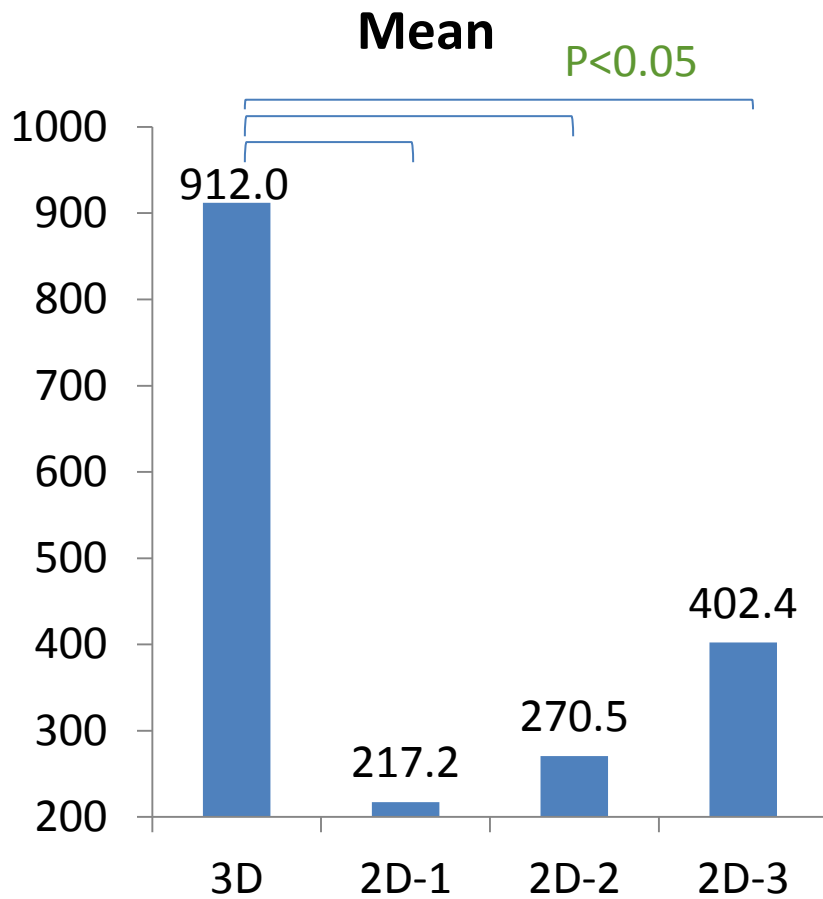
## Total Lesion Volume

(Primary Endpoint for Most TAVR DW-MRI Studies)

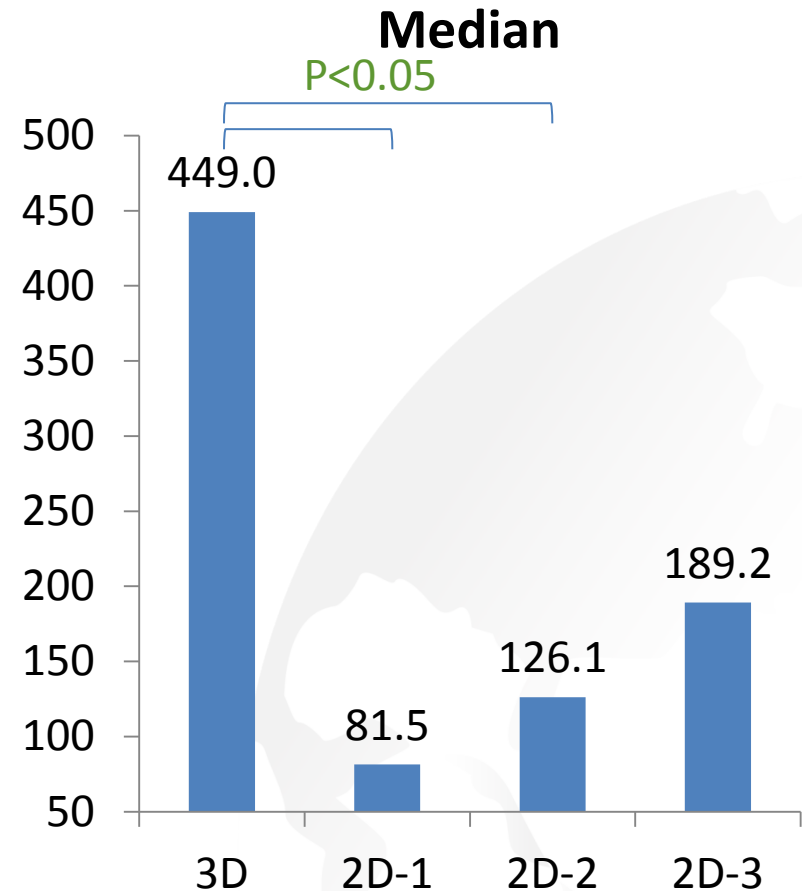


# Results

## Total Lesion Volume



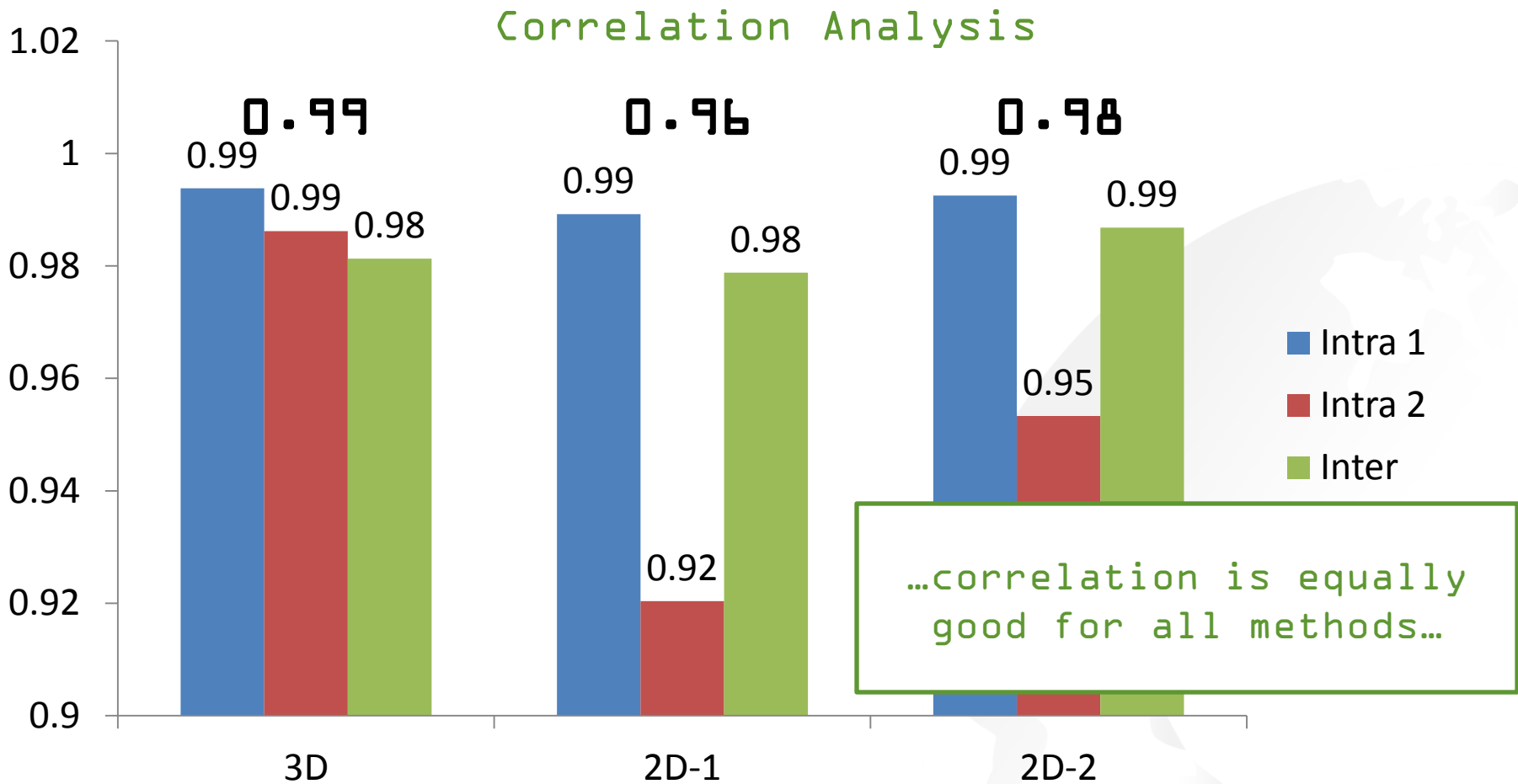
ANOVA p-value:  $< 0.001$



K-W p-value: 0.01035

# Results

## Total Lesion Volume

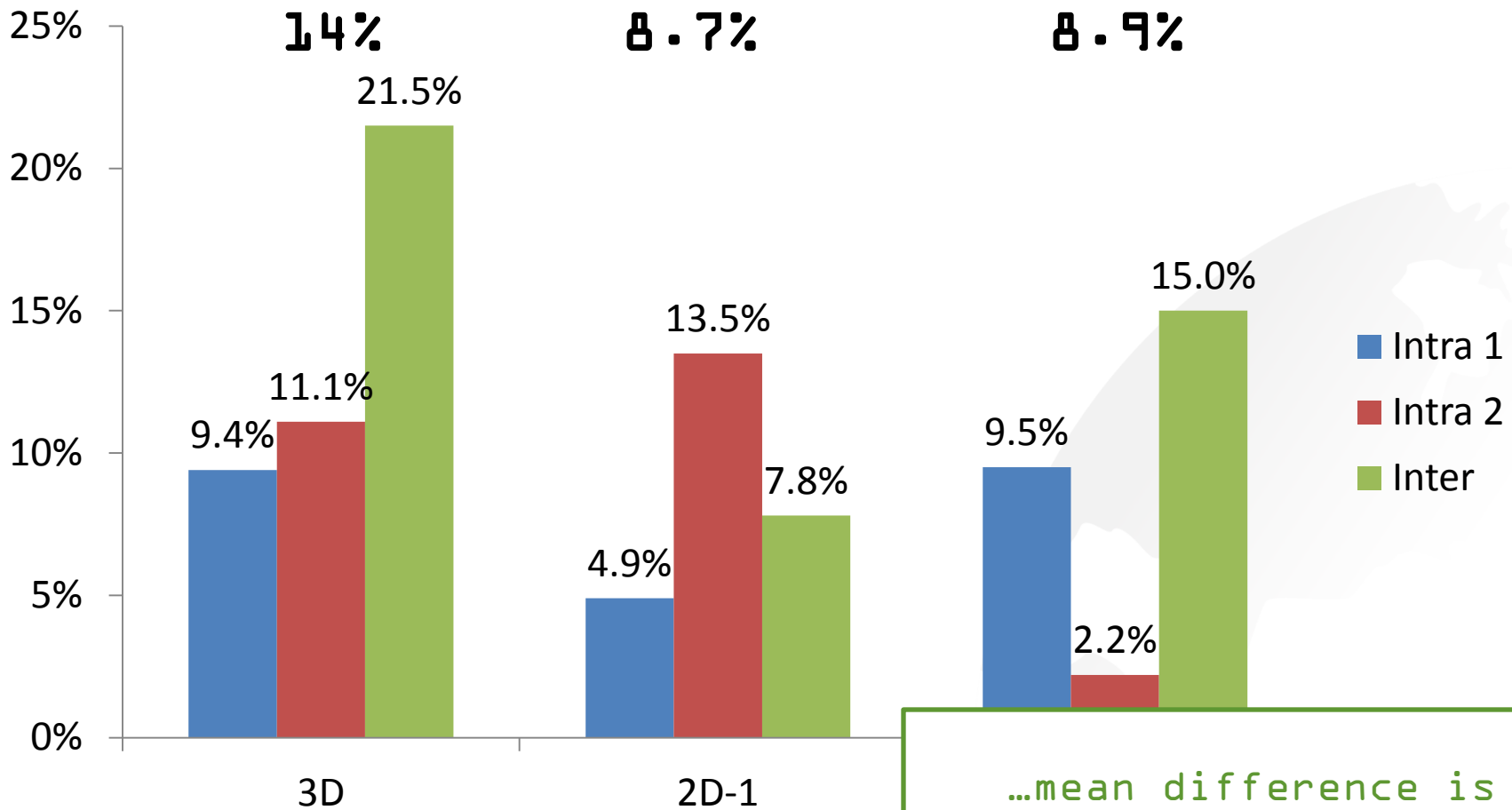


# Results

## Total Lesion Volume



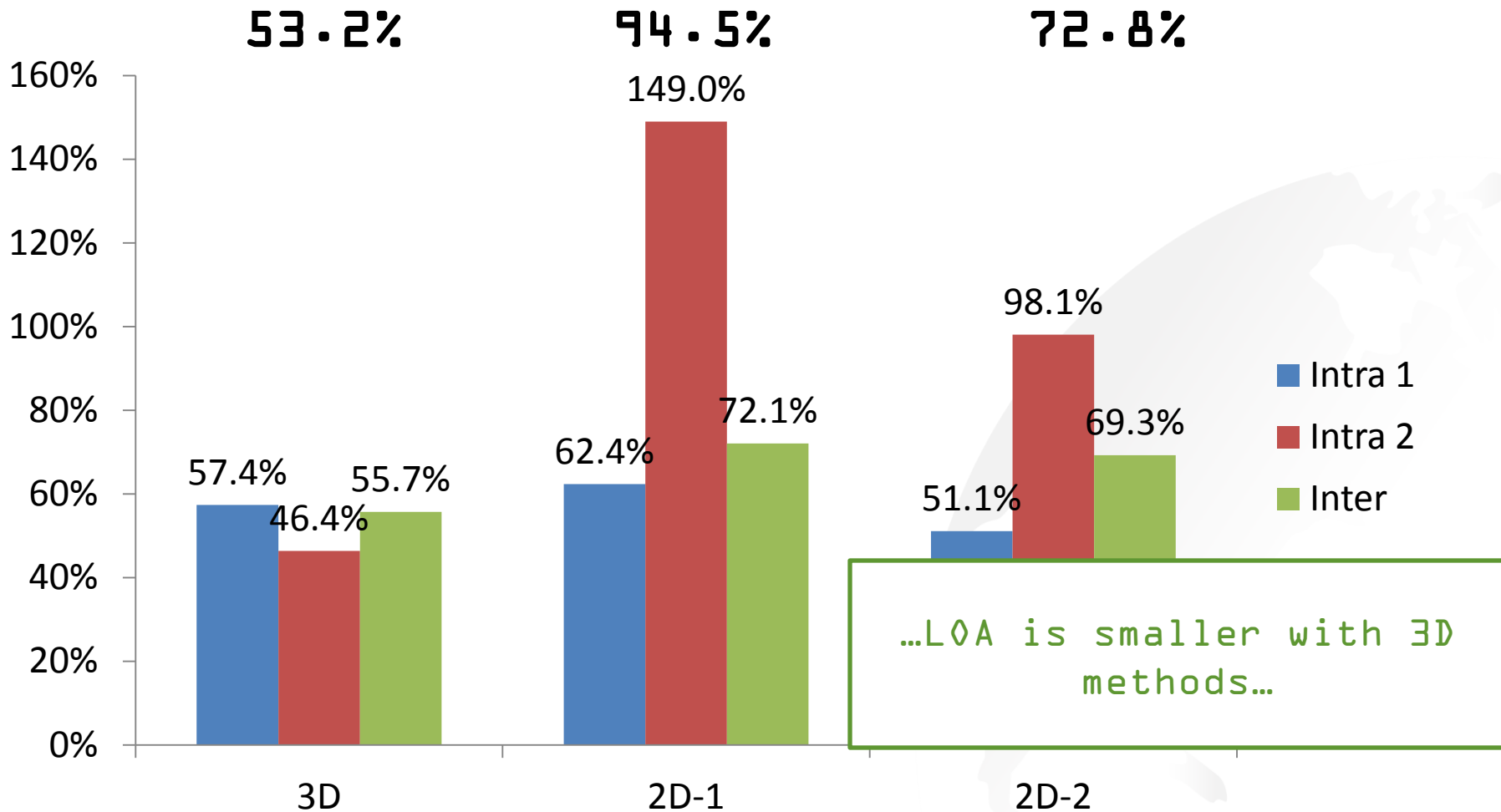
### Bland-Altman Analysis: Mean Difference



# Results

## Total Lesion Volume

Bland-Altman Analysis: Limits of Agreement





# Results

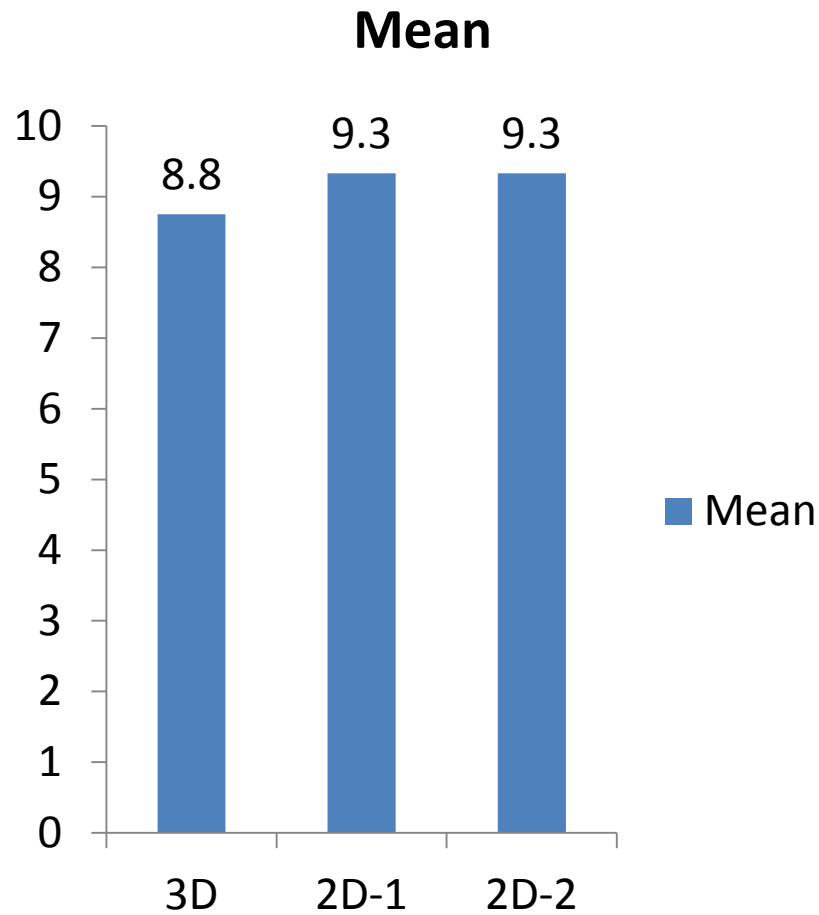


**Lesion Number**

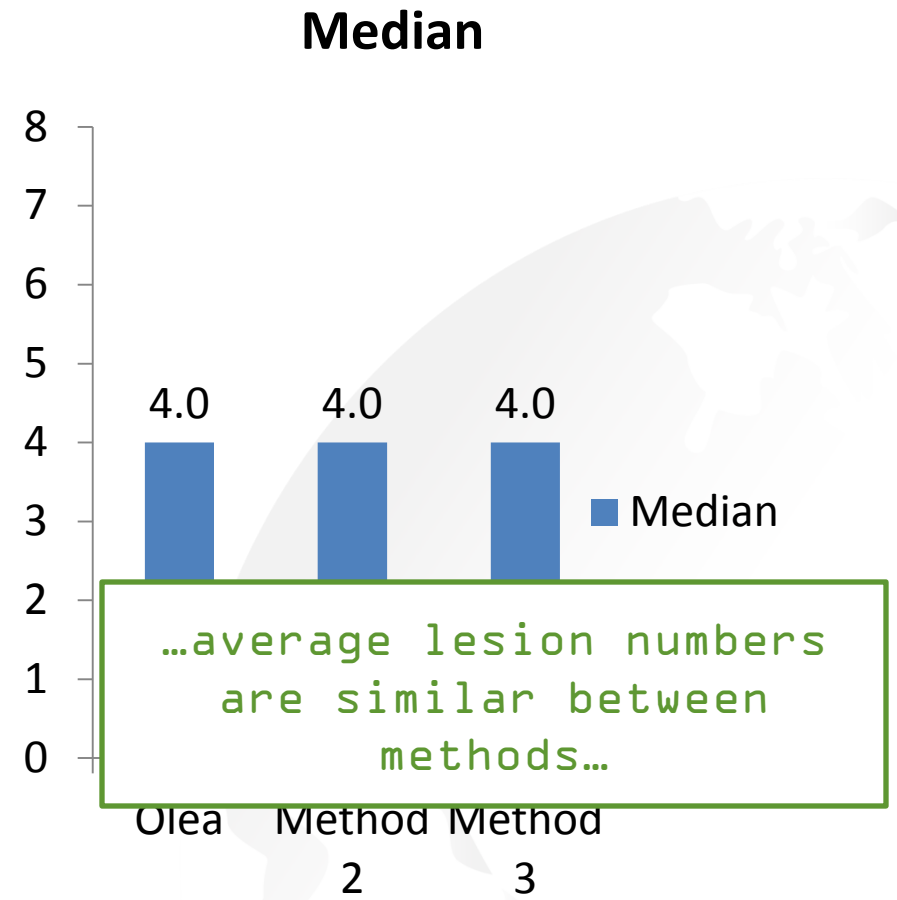


# Results

## Lesion Number



ANOVA p-value: 0.969

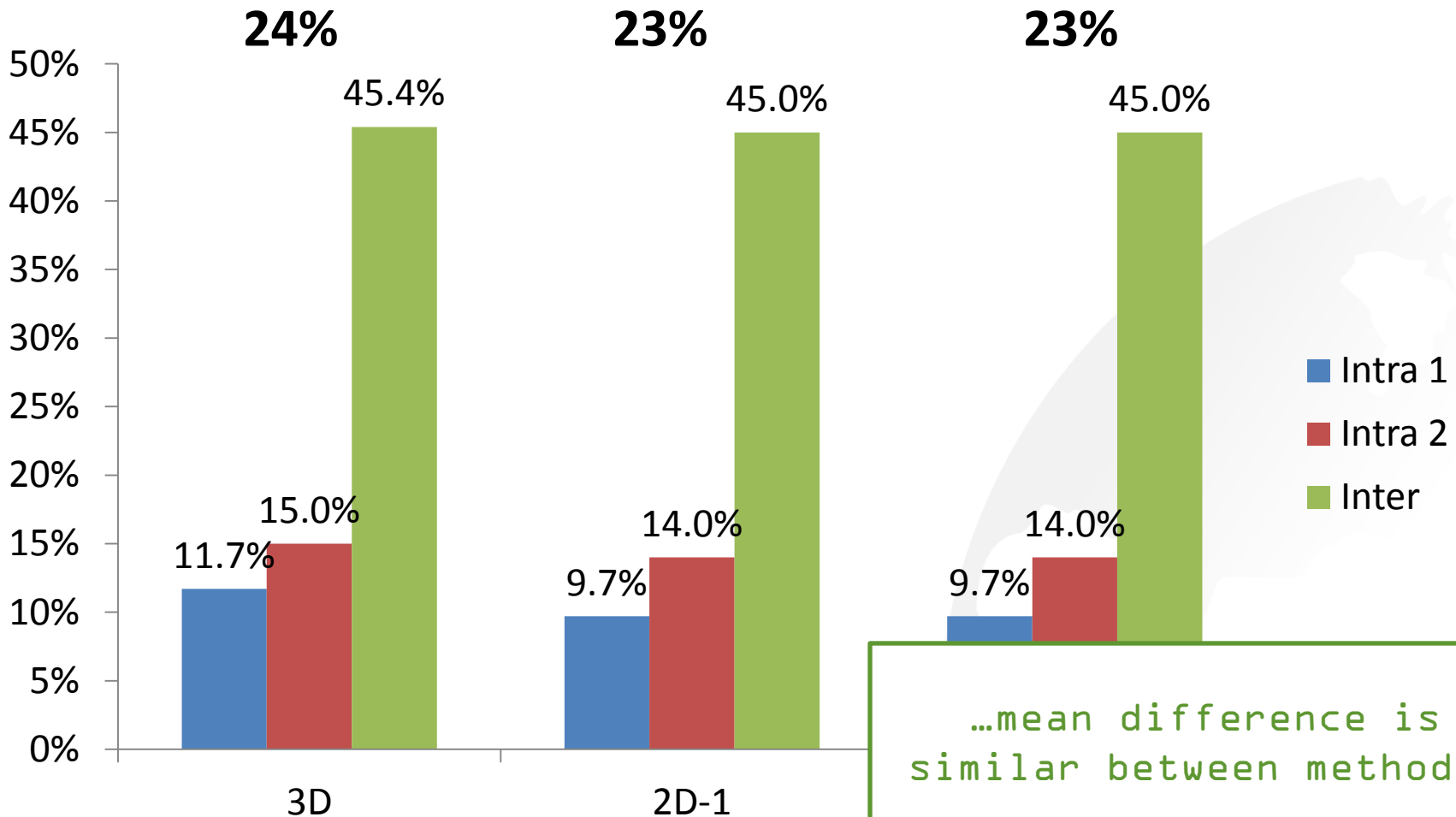


K-W p-value: 0.9917

# Results

## Lesion Number

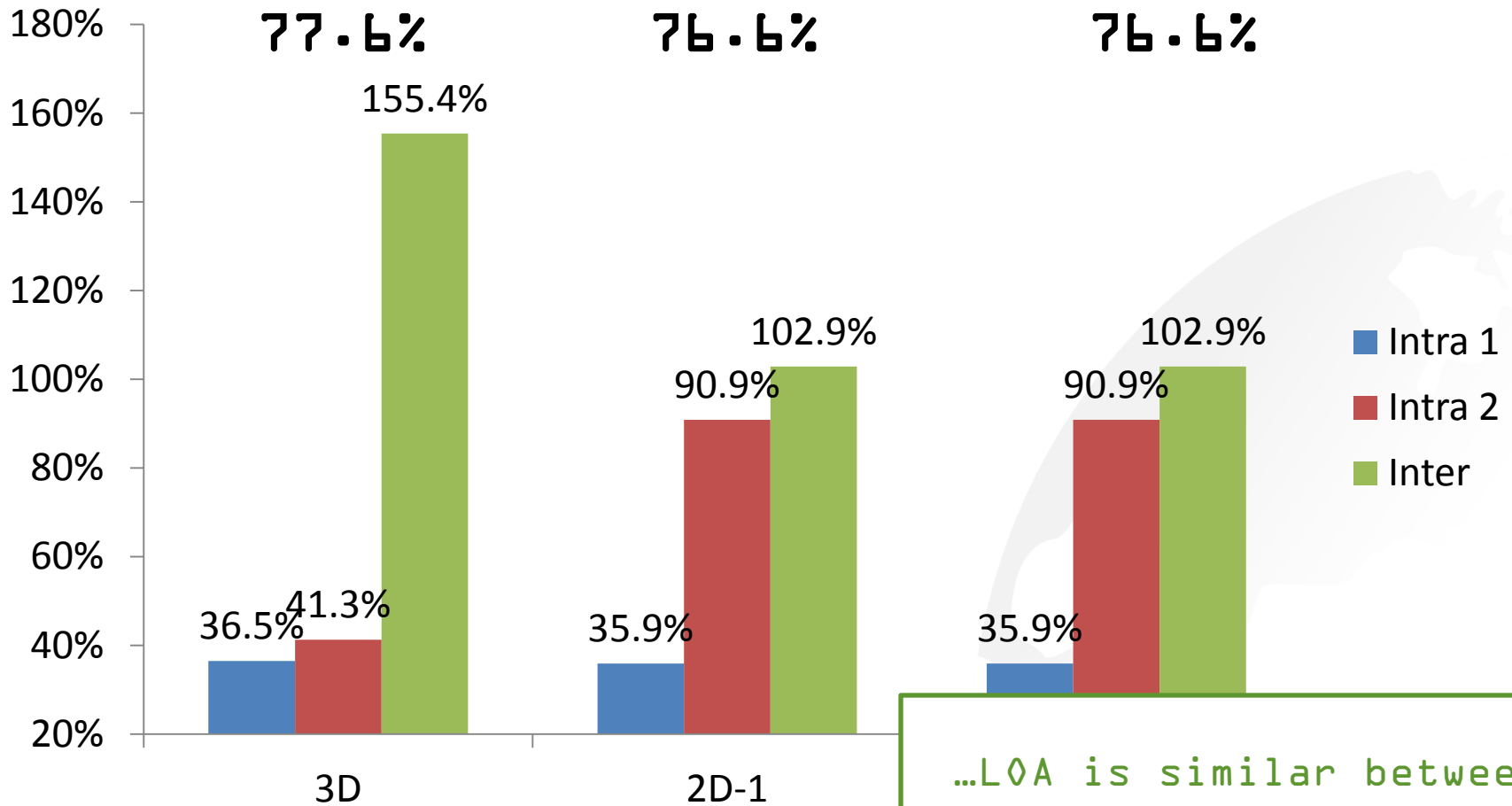
### Bland-Altman Analysis: Mean Difference



# Results

## Lesion Number

### Bland-Altman Analysis: Limits of Agreement



# Summary




1. To our knowledge, this is the first systematic study to assess the methodology of quantifying cerebral DW-MR lesions
2. Total lesion volumes are significantly higher with 3D methods, compared to 2D methodologies
  - This could have a major impact when comparing total lesion volumes across different studies, as recent and current ongoing studies use a 2D method
3. Reproducibility of 2D and 3D methods are excellent and comparable
  - Particularly, the ABC/2 method is reproducible, easy to use and most widely published

# Conclusion



...quantification of cerebral DW-MRI lesions in the context of TAVR-related clinical trials may be best accomplished by 2D-methods, as these methods have good reproducibility and are widely used in the literature and ongoing clinical trials...

...the ABC/2 method is easy, reproducible and widely used...



# Impact of MRI Methodology on DWI MRI Lesion Volume Measurements and Statistical Implications

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