

AIRAscore 2.1.0

# Instructions for Use



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# 1 Customer Information

Dear customers,

You have decided to support your reporting by using the AIRAscore software. We would like to thank you for this decision. The AIRAscore software is a certified medical device with CE marking according to council directive (EU) 93/42/EEC, which is placed on the market in accordance with transitional provisions of regulation (EU) 2017/745 on medical devices. AIRAmEd has established a quality management system according to ISO 13485 and is certified therefor.

This customer information applies as instructions for use, describes the basic features of our evaluation report and provides information on the correct use of AIRAscore. It describes the correct indication, the appropriate reference set, and basic warnings that must be followed. The customer information is intended for all physicians with knowledge of MR anatomy of the brain who use the AIRAscore report to check segmentations and place the output measurements in the clinical context (primary users).

All users and administrators of the software who use the software or install and maintain it must have access to these instructions for use and be familiar with their contents.

If you have any questions beyond this customer information, please do not hesitate to contact us:

service@airamed.de

<https://www.airamed.de>

phone number: +49 7071 53 933 40



## 2 General Customer Information

### 2.1 General Specifications

It is your responsibility as the user to inform the patient of the service and the associated transfer of image data to AIRAmEd and to take appropriate local protective measures to prevent unauthorized third parties from accessing AIRAmEd's service and patient data.

#### 2.1.1 Intended Purpose

AIRAscore provides automated, fast and reliable segmentation of brain volumes into gray matter, white matter and CSF as well as additional anatomical mapping. AIRAscore analyzes MRI datasets based on deep learning techniques. By providing absolute volume data and relative volume data compared to total intracranial volume, the data can be compared and classified against an age- and sex-matched reference set.

#### 2.1.2 Clinical Benefit

The software thus supports physicians in the diagnosis and therapy monitoring of neurodegenerative diseases, as regional atrophy patterns can be detected and this enables a temporal assessment of the progression of atrophy. The software supports the radiologist in the evaluation of complex and subtle image findings and thus increases diagnostic certainty.

#### 2.1.3 Indication

Typical areas of application are therefore the diagnosis of dementia (ICD-10 F00-F03), but also the assessment of atrophy in patients with multiple sclerosis (ICD-10 G35). For patients with suspected multiple sclerosis (ICD-10 G35), a detailed assessment of lesion burden is possible.

AIRAscore may be used with image data of individuals between the ages of 18 and 85.

#### 2.1.4 Availability

AIRAscore is usually available 24 hours a day and operates fully automated.

We usually perform scheduled maintenance Monday through Friday from 0:00 to 4:00 or all day on weekends. Scheduled maintenance is announced at least 24 hours in advance. Unscheduled maintenance can be performed at any time without notice if the security of the system is affected.

We keep downtime as low as possible, as long as it is within our control.

If you have any questions, our support is available Monday through Friday from 9:00am to 4:00pm by phone or email.

#### 2.1.5 Target Patient Group

The AIRAscore structure report is aimed at patients between the ages of 18 and 85 who are suspected of having a disease associated with increased brain tissue loss (atrophy).

For patients suffering from multiple sclerosis, the software can additionally be used to determine the total lesion volume as well as the number of lesions. For this instance, the report AIRAscore MS should be used, which offers additional analyses for multiple sclerosis.

#### 2.1.6 Contraindications, Avoidable Misuse and Abnormal Use



- AIRAscore is not suitable for evaluating image data that is not based on a T1 data set.
- Image datasets after administration of contrast agents are not suitable for evaluation and may lead to erroneous findings.
- Any mass lesion (e.g., tumor, hemorrhage, arachnoid cyst, etc.) or any lesion that is characterized by a defect of the brain tissue (e.g., defects after trauma, ischemia, etc.) may lead to severe missegmentation and also cannot be evaluated against the reference set.

Corresponding patient image data must NOT be evaluated with AIRAscore!



⚠️ Age and natural sex of the patients are essential for a correct classification of the volumes. Changes to the DICOM metadata should therefore be avoided, since AIRAmed has no possibility to check the correctness of the DICOM data. In the case of anonymized data or research data, it is therefore essential to ensure that age, gender and the interval between examination date and date of birth are correctly preserved in the DICOM data.

⚠️ Reports of the same patient are only comparable with regards to the progression if they were acquired with the same scanner and the same sequence. Even minor changes in scan parameters can lead to strong contrast changes and discrete shifts in the gray-white boundary, which make segmentation comparability impossible. Information on measurement inaccuracy due to rounding can be found in the customer note of each evaluation report on the last page.

⚠️ The quantitative evaluation of brain structures can only support the assessment and diagnosis by a qualified physician (specialist), and by no means replaces it.

### 2.1.7 Ordering AIRAscore MS

In order to add the multiple sclerosis analysis to the general AIRAscore structure report, we need a T2 FLAIR dataset in addition to a T1 dataset. After installing our software (see AIRAscore Client Installation Instructions), two new PACS nodes will be available, the names of which will be determined by the person doing the installation. The node for the AIRAscore structure report will only accept T1 datasets and will start processing immediately if a valid dataset is found. The node for AIRAscore MS expects a T1 dataset as well as a T2 FLAIR dataset that meet the requirements listed in the next paragraph. You can send the datasets in any order, but there should be no more than two hours between the two datasets, otherwise the job will be discarded.

### 2.1.8 Technical Requirements for the Dataset

To process your image data, AIRAscore structure requires datasets with the following properties:

- T1 dataset, native, DICOM format: *MR Image IOD*
- Clear gray-white contrast between gray and white matter and, if possible, hypointense representation of CSF (for accepted parameter combinations, please refer to Part II)
- 3D dataset
- Device manufacturer: GE, Philips or Siemens
- Field strength: 1.5 or 3 Tesla
- Resolution of image data in each spatial direction < 2mm and voxel size  $\leq 2.4 \text{ mm}^3$
- The head must be completely captured
- The head should not be captured tilted if possible
- No pronounced artifacts should be visible in the image (motion, folding, etc.)

If you decide to use AIRAscore MS, we require a corresponding T2-FLAIR dataset with the following properties in addition to each T1 dataset:

- T2-FLAIR DICOM dataset, DICOM format: *MR Image IOD*
- 2D or 3D dataset
- Device manufacturer: GE, Philips or Siemens
- Field strength: 1.5 or 3 Tesla
- Resolution of image data  $\leq 1.5 \text{ mm}$  in x and y direction and  $\leq 6 \text{ mm}$  in slice direction
- The head must be completely captured
- The head should not be captured tilted if possible
- No pronounced artifacts should be visible in the image (motion, folding, etc.)


For a detailed list of all requirements for DICOM data, please refer to the separate DICOM Conformance Statement.

### 2.1.9 Automated Control of Image Data and Accountability of the Requesting Physician

All image data are automatically checked after being received by AIRAmed. For this purpose, in addition to the actual image data, the technical data of the sequence, the age and the gender of the patient from the DICOM header are transferred. Other patient-related data, such as the name, are not transmitted to AIRAmed and remain locally and encrypted on your system. The majority of possible technical errors are detected automatically. However, this does not exclude the residual risk that datasets for which the technical requirements are not met or datasets of



patients with contraindications are nevertheless processed. Also, despite all due care, incorrect segmentation may occur in rare cases.


 All reports must be **checked** for plausibility and accuracy by a **qualified physician** (specialist) with sufficient knowledge of neuroanatomy and MR imaging of the head before they are used for clinical assessment and diagnosis. This includes all reports used for longitudinal comparisons. The identity of the patient should also be checked.

The original images are overlaid with the results of the segmentations (anatomy and tissue) performed by AIRAscore structure. These are displayed in the report for verification purposes. If you have ordered AIRAscore MS, the segmentation of lesions and their categorization into juxtacortical, periventricular and infratentorial will be presented in a similar way. In addition, the segmentations are provided in the PACS. The hippocampus is reported as a distinct structure. The hippocampus and cingulate gyrus are not included in the frontal or parietal lobes.

For viewing you need a PACS and a connected DICOM viewer including a monitor that can display the DICOM formats *Encapsulated PDF IOD* as well as *Secondary Capture Image IOD* in color and is approved for reporting.

As a rule, you will receive the results within a few minutes, although the actual time also depends on your Internet connection. If you do not receive an evaluation within one hour after sending the data, please contact us directly. In rare cases, datasets may not be sent to us, or may not be sent completely, and thus processing may not take place.

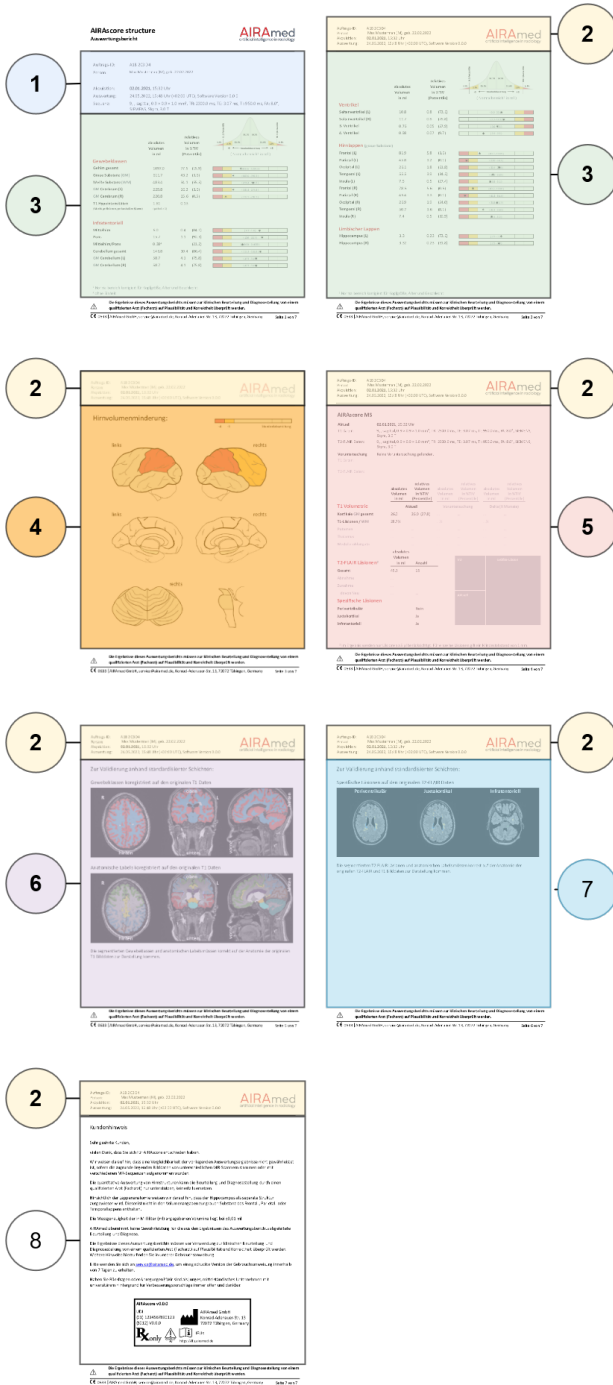
If you are of the opinion that there is a safety-relevant malfunction in the product, please contact our customer service immediately.

 AIRAm

ed does not assume any warranty for the assessment and diagnosis derived from the evaluation results of the evaluation report and cannot be held liable for this.



2.1.10 Structure of the Report



The AIRAscore structure report has 5 pages, and 7 pages with AIRAscore MS. The respective page number is listed on the bottom right.

The individual sections of the report are described below:

- ① Examination Summary:  
 Contains the order ID\*, personal data of the patient and the sequence on which the report is based.
- ② Headers:  
 The headers also list the most important identification parameters and relevant data again.
- ③ Volume Report:  
 Contains the volume evaluation for each segmented anatomical area with the raw value in ml, the relative value with respect to the total intracranial volume and the percentile for the patient compared to the reference set\*\*.
- ④ Visualization of Atrophy Areas:  
 Quick overview of potential volume reductions. Areas with volume reductions compared to the reference set are shown here in yellow or red\*\*.
- ⑤ MS Report:  
 This page is optional and is only issued to customers requesting AIRAscore MS. It shows the number and volume of lesions and their categorization.
- ⑥ Quality Control Images:  
 The quality control images are used for the traceable validation of our segmentation results. These quality control images must always be checked for plausibility. In the event of discrepancies or inexplicable volume data, the plausibility of the overlays provided in the PACs should also be checked.
- ⑦ MS Control Images:  
 This page is optional and is only issued to customers requesting AIRAscore MS. It displays slices with the largest juxtacortical, periventricular and infratentorial lesions for reference.
- ⑧ Customer Notices:  
 The customer notices contain information on the use of the report, the accuracy of the results and contact options for AIRAmEd GmbH.







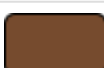
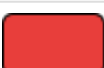
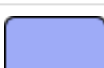

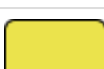

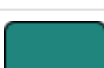







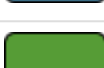
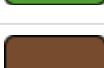

**i** \* The individual order ID allows us to make a reliable assignment if required. Apart from the pseudonymized order ID and the pure image data as well as age and gender for the assignment of the correct reference values, AIRAmEd does not store any personal data in the image archive. Without individual order ID of your patients, no assignment of image data in the long-term archive or in our log files is possible. All our processes meet the requirements of the GDPR.

\*\* If the patient age is not between 18 and 85, no comparison to the reference set will be performed and the percentile will not be shown in the report. The page “Visualization of Atrophy Areas“ will be omitted. Furthermore, a watermark “Not released for clinical evaluation“ will be shown in the report, if the patient is younger than 18 years.

### 2.1.11 Color-coded Segmentation Results







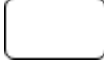













Several DICOM series are also available for visual control. All customers receive the two DICOM series Anatomy Map and Tissue Map. Customers requesting AIRAscore MS receive an additional DICOM series T2-Lesion Map. All available series can be found in the same study as the PDF report. If there are several segmentations, you can identify the correct assignment via the name of the initial series. The segmentation results are color-coded in this.

#### 2.1.11.1 AIRAscore structure Segmentation Results:

Anatomical Region	Anatomical Sub-Region		Color in “Anatomy Map”	Color in “Tissue Map”	
Brain total	Gray Matter	GM Cerebrum (L)	Temporal left		
			Hippocampus left		
			Parietal left		
			Frontal left		
			Occipital left		
			Insula left		
			Gyrus cinguli left		
		GM Cerebellum (L) *			
		GM Cerebrum (R)	Temporal right		
			Hippocampus right		
			Parietal right		
			Frontal right		
			Occipital right		





Anatomical Region	Anatomical Sub-Region		Color in "Anatomy Map"	Color in "Tissue Map"	
		Insula right			
		Gyrus cinguli right			
		GM Cerebellum (R) *			
		Deep gray matter (Basal Ganglia)			
	White Matter	Pons			
		Midbrain			
		Superior cerebellar peduncle **			
		Remaining white matter	N/A		
		T1 Hypointensities		N/A	
	CSF spaces	Lateral ventricle left			N/A
Lateral ventricle right			N/A		
3. ventricle			N/A		
4. ventricle			N/A		
Outer CSF space		N/A	N/A		

"N/A" - The corresponding region is not marked with a color







\*) Total cerebellum: combination of gray and white matter of the segmented cerebellum


\*\*\*) The volume of the superior cerebellar peduncle is not shown in the report due to the size-related measurement inaccuracies

#### 2.1.11.2 AIRAscore MS Segmentation Results:

Structures	Color	Comments
Total Cortical GM	N/A	Volume = Total GM Cerebrum



T2-hyperintense lesion	Periventricular lesion		Voxel of a lesion that borders the ventricle
	Juxtacortical lesion		Voxel of a lesion that borders with the cortical ribbon
	Infratentorial lesion		Voxel with an infratentorial position
	Unspecific lesion		Voxel associated with a T2 hyperintense lesion

 "N/A" - The corresponding region is not marked with a color

### 2.1.12 Report Language

The report can be returned in one of the languages listed below. To change the configured language, please refer to AIRAscore Client Installation Instructions, section "Country Code".

The formatting of the following information in the report is affected by the configured country code:

Country Code	Language	Patient Name Format	Date Format	Time Format
en_US	English	First_Name Last_Name	Mon dd, yyyy	AM/PM
de_DE	German	Last_Name, First_Name	dd.mm.yyyy	24-hour clock (military time)

### 2.1.13 Precision and Accuracy

All metrics used for the precision and accuracy calculations are listed in the following. All metrics were calculated with milliliter as unit.

- ICC: intraclass correlation coefficient
- Median of absolute differences between volume measurements
- IQR: interquartile range
- p90: 90th percentile
- Correlation: Pearson's correlation coefficient
- Sensitivity
- Precision

The precision of AIRAscore structure was calculated through the evaluation of a Test-Retest dataset consisting of 392 samples. The median ICC across all regions was 0.99. For all regions, AIRAscore structure achieved a higher ICC as the comparable software tools FreeSurfer and SPM12.

Precision of AIRAscore structure	
Metric	Value
Median ICC	0.99
p90 ICC	0.99
Average of region-wise median of absolute volume differences	0.26
Standard deviation of region-wise median of absolute volume differences	0.29

The precision of lesion segmentations with AIRAscore MS was calculated using a dataset of 19 Test-Retest samples.

Precision of AIRAscore MS
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Metric	ICC	Median	IQR	p90
Total lesion volume	0.999	0.085	0.105	0.252
Lesion count	0.996	2	1.5	3

The accuracy of AIRAscore structure was evaluated by comparison with 20 samples that were manually segmented by experts. The average correlation of volumes between AIRAscore structure segmentations and manual segmentations across all regions is 0.82 (+/- 0.16). All regions fulfilled the acceptance criteria.

Accuracy metrics for AIRAscore MS were calculated by comparison to manual segmentation by experts of 10 samples from patients with MS. The sensitivity and precision of the total lesion count is 70% and 72%, respectively. The median absolute volume deviation is 1.05 milliliter.

### 2.1.14 Diagnostic Accuracy

AIRAscore was able to identify patients with Alzheimer on a data set of 23 healthy controls and 46 Alzheimer patients aged 55 to 85 years based on the volumetry of the temporal lobes and hippocampus. The sensitivity and specificity for the z-values of -2 and -3 displayed in the report for hippocampus (at least one hippocampus <= cut-off) was 85% and 96% or 61% and 100% respectively, and for the temporal lobe (at least one temporal lobe <= cut-off) 72% and 100% or 46% and 100% respectively. The combination of temporal lobe and hippocampus achieved a sensitivity and specificity of 87% and 96% at -2 and 76% and 100% at -3.

In the course of the disease the sensitivity increased after one year. The sensitivity and specificity for the z-values of -2 and -3 displayed in the report for hippocampus (at least one hippocampus <= cut-off) was 88% and 95% or 69% and 100% respectively, and for the temporal lobe (at least one temporal lobe <= cut-off) 83% and 100% or 57% and 100% respectively. The combination of temporal lobe and hippocampus achieved a sensitivity and specificity of 93% and 95% at -2 and 76% and 100% and -3.

## 2.2 Installing AIRAscore Client

AIRAmEd provides you, the customer, with the AIRAscore Client software. The AIRAscore Client operates as the interface to AIRAmEd's servers. For instructions how to install AIRAscore Client, please refer to the AIRAscore Client Installation Instructions, which will be provided to you by AIRAmEd.

## 2.3 Known Problems

In the case of a transfer of DICOM image data that does not meet the technical requirements, the rejection is currently only saved in the log file and no further notification is given. The log file can usually be viewed by the person who performed the installation. Where the log files are located and how they can be accessed is explained in more detail in the AIRAscore Client Installation Instructions, section Accessing AIRAscore Client Logs.

The DICOM PatientOrientation field is set as an empty field for the segmentation results. However, the ImageOrientation (Patient) [0020,0037] and ImagePosition (Patient) [0020,0032] fields contain the relevant information.

The DICOM field IssuerOfPatientID contains the value *None* if it was not set in the input data.

## 2.4 Obligation to report (only for EU-countries)

Please report all serious incidents (harms, injuries, etc) related to this medical device to the manufacturer and the responsible authority of the EU member state, that you are established in.

In Germany the responsible authority is the BfArM. The latest contact information can be obtained from the BfArM website at: <https://www.bfarm.de>.

## 2.5 Querying the UDI

The Unique Device Identification (UDI) for AIRAscore can be obtained by accessing the following URL: [https://api.airamed.de/v1\\_0/udi](https://api.airamed.de/v1_0/udi). The response will include the UDI-DI (Device Identifier) as well as the UDI-PI (Production Identifier).



### 3 About AIRAscore Client

AIRAscore Client is used to connect to the AIRAscore software and is developed by AIRAm ed GmbH. All rights reserved.

AIRAscore Client uses the [Requests](#) library, Copyright 2019 Kenneth Reitz, in version 2.26.0.

AIRAscore Client uses [Watchtower](#), Copyright 2021 Simon Aronsson, in version 1.3.0.

AIRAscore Client uses the [fpdf2](#) library, Copyright 2013 Lucas Cimon, in version 2.5.1.

