Original Article

Baseline MRI Examination in the NAKO Health Study

Findings on Feasibility, Participation and Dropout Rates, Comfort, and Image Quality

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Summary

Background: Magnetic resonance imaging (MRI) yields important information on the development and current status of many different diseases. Whole-body MRI was accordingly made a part of the multicenter, population-based NAKO Health Study. The present analysis concerns the feasibility of the baseline MRI examination and various aspects of quality assurance over the period 2014–2019.

Methods: 32 252 participants in the NAKO Health Study, aged 20 to 74, who had no contraindication to MRI were invited to undergo scanning in one of five MRI study centers across Germany. The whole-body MRI scan took about one hour and consisted of sequences for the visualization of structural and functional features of the brain, musculoskeletal system, cardiovascular system, and thoracoabdominal system. A comprehensive quality-assurance assessment was carried out, with evaluation of adverse events, the completeness of the MRI protocols, the participants' subjective perceptions, and image quality.

Results: 31 578 participants (97.9%) were successfully included in the MRI study. They reported a high level of comfort and suffered no severe adverse events (mild adverse events occurred in only four participants). Depending on the imaging sequence, the image quality was rated as excellent in 80.2% to 96.8% of cases. Quality assessment with respect to structural features of the brain revealed high consistency across study centers, as well as with regard to age- and sex-based differences in brain volume (men, 1203.81 ± 102.06 cm^3; women, 1068.10 ± 86.69 cm^3).

Conclusion: Whole-body MRI was successfully implemented in the NAKO baseline examination and was associated with high patient comfort and very good image quality. The imaging biomarkers of the brain confirmed previously observed differences based on age and sex, underscoring the feasibility of data pooling.

Cite this as:
Bamberg F, Schlett CL, Caspers S, Ringhof S, Günther M, Hirsch JG, Rüdebusch J, Miklánková P, Bittner N, Jockwitz C, Forsting M, Hosten N, Kaaks R, Kauczor HU, Kroenke T, Niendorf T, Peters A, Pischon T, Stang A, Berger K, Völzke H, NAKO Investigator Consortium: Baseline MRI examination in the NAKO Health Study—findings on feasibility, participation and dropout rates, comfort, and image quality. Dtsch Arztebl Int 2024; 121: 587–93.
DOI: 10.3238/arztebl.m2024.0151

The technological advances in magnetic resonance imaging (MRI) over the past few decades have given it a central role in modern medicine (1). Although specialized training, expertise, and a professional framework ere required (2, 3), this investment of resources is well justified in the age of personalized medicine. The excellent images obtained by MRI provide high-resolution delineation of tissue morphology and function and of potential disease states (4). Given these features, MRI is increasingly being used in research settings to throw more light on the development of common diseases (5, 6).

One of the largest population-based cohort studies in the European Union is the NAKO Health Study. As part of the NAKO baseline examination, a total of 205 415 participants were examined in 18 study centers across Germany between 2014 and 2019 (7, 8). They all underwent various examinations and were followed up prospectively over time. One of the most innovative aspects NAKO Health Study was the whole-body MRI examination, which was performed at five MRI study centers in a subset of over 30 000 participants (9). In order to maximize internal validity and also minimize potential bias between imaging and non-imaging parameters, the employed MR techniques and protocols were state-of-the-art and followed strict standard operating procedures. Various measures and checks were applied for quality assurance. Based on comprehensive ethical considerations (10), all images were read by board-certified radiologists for incidental findings in a standardized fashion (11–13).

While MRI is solidly established in the clinical context, it has not previously been

used in a long-term multicenter population study has not been accomplished in Germany, and thus, the performance quality in this setting remains unknown. The aim of the present study was therefore to analyze the feasibility of whole-body MRI as part of the NAKO baseline examination, including participation and dropout rates, as well as participant comfort and image data quality.

Methods

Study design and population

The NAKO Health Study was designed as a prospective cohort study. A total of 205 415 participants aged 20–69 years, selected randomly from compulsory registries of residents within the study areas (8), underwent a highly standardized examination program (labeled L1) of 4 hours' duration (7). Approximately 20% of all individuals, randomly selected prior to invitation, spent about an additional 1 hour undergoing further examinations, including more in-depth medical tests (labeled L2) (8).

As part of the MRI baseline examination, L2 participants from 11 of the 18 NAKO study centers were also invited to participate in a whole-body MRI examination. They were recruited at five imaging study centers (Augsburg, Berlin, Essen, Mannheim, Neubrandenburg) and 6 adjacent study centers (Berlin Central, Berlin South, Düsseldorf, Freiburg, Münster, Saarbrücken), from where they were sent to the nearest MRI study centers.

Persons were considered eligible if no contraindications were present and they were willing to participate in the MRI examination taking approximately 1 hour (for the exclusion criteria see *eBox 1*). The MRI study was approved by the Bavarian State Medical Association and the local ethics committees. Written informed consent was obtained from all participants prior to the examination.

Medical Resonance imaging program

MRI examinations were performed on five study-dedicated 3-T MR systems (MAGNETOM Skyra, Siemens Healthineers, Erlangen, Germany) with identical hardware and software components. The applied MRI program was also identical at all sites and was overseen by local board-certified radiologists. It comprised four organ areas: brain, musculoskeletal system, cardiovascular system, and thoracoabdominal system (9). Following the examination, participants were discharged without feedback (blinded) and the MR images were reviewed by board-certified radiologists for the presence of incidental findings according to a predefined list (14).

In order to assure high study and image quality, a so-called MRI Core of four centers was established to take responsibility for the planning, conduct, monitoring, and completion of all MRI-related study procedures. These centers were: University Hospital Freiburg (coordination and training), University Hospital Heidelberg (incidental findings), MEVIS Bremen (data management), and University Medical Center Greifswald (quality assurance).

Side effects, safety, and comfort

At each of the five MRI study centers, one dedicated radiologist monitored the various aspects of the MRI study. This included the clarification of exclusion criteria, dealing with questions that raised by participants, and providing any support necessary during the image acquisition process. Self-reported side effects and adverse events were documented prospectively by the MRI study centers.

Five surveys of satisfaction were carried out at 6-month intervals between fall 2016 and fall 2018. Each time, 100 questionnaires were distributed at each of the five study centers. Altogether, therefore, a subgroup of 2500 participants were asked about their satisfaction with the study program on a voluntary basis. The topics concerned were satisfaction with the consent process, the overall procedure at the MRI study center, and the duration of the MRI examination. Responses were given on a five- or three-point Likert scale.

MRI image quality

MR image quality was assessed subjectively by certified radiologists on a three-tier scale according to predefined quality criteria. Furthermore, a series of image-based quality measures were derived fully automatically (15), e.g., common values (signal-to-noise ratio, sharpness, etc.) and artifact- and protocol-specific parameters (16, 17). More details are provided in the eSupplement

Statistics

For the present analyses we used an exploratory approach without formal testing of hypotheses and without defining a formal level of statistical significance.

For further evaluation of image quality a state-of-the-art imaging pipeline was used that enabled estimation of morphometric parameters (total brain volume, white matter and gray matter volume, and cerebrospinal fluid volume) from T1w images. The images were processed using FreeSurfer (v7.1.1, recon-all pipeline for surface reconstruction [18, 19]) and CAT12.8 (20). The extracted variables were additionally corrected for height and weight and were classified by age, MRI study center, and biological sex.

We used SAS (Version 9.5) and NIST DataPlot (National Institute of Standards and Technology, Gaithersburg, MD, USA) for statistical analyses.

Results

A total of 32 252 participants were invited to attend one of the five MRI study centers for whole-body MRI examination. Of these, 641 participants (2.0%) were excluded from the study due to contraindications and 33 participants (0.1%) decided not to take part. Ultimately, 31 578 participants (97.9%) gave their written informed consent and were included for MRI examination. *Table 1* shows the sample characteristics stratified by study site. Overall, a slight majority of participants were male (56.0%). The participants' age on the day of the examination ranged from 20 to 74 years (49.0 ± 12.3 years).

Completeness of the MRI data set

Of the participants included for MRI, 710 withdrew their participation during the first MRI sequence, resulting in a dropout rate of 2.2% and a total of n = 30 868 participants (95.7%) with at least one complete MR scan. The full MR protocol with all 16 sequences was completed in 29 757 participants (92.3%).

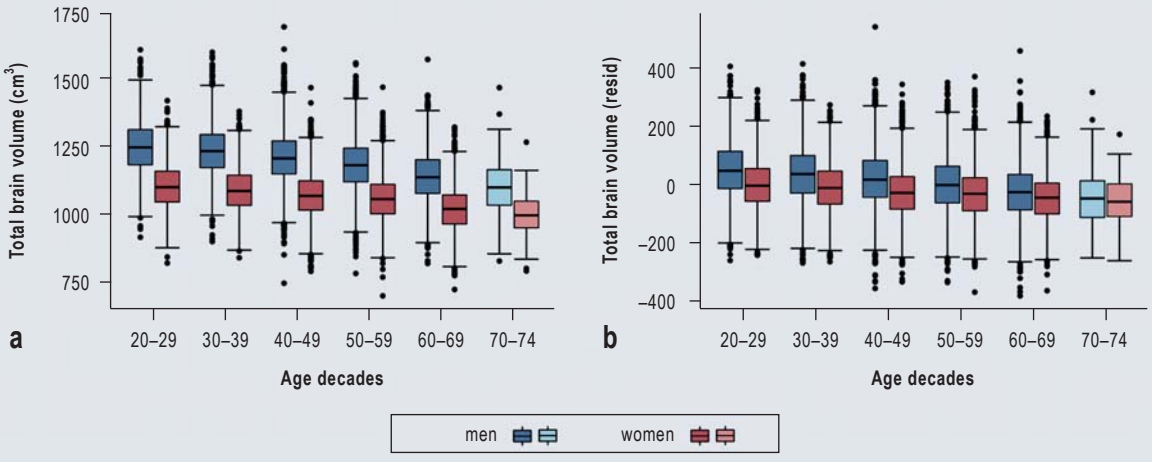
Table 1

Demographic data of the participants in the whole-body MRI study in the NAKO Health Study

Variable	Total	Augsburg	Berlin	Essen	Mannheim	Neubrandenburg
n	31 578	6417	5980	6155	6021	7005
Women, n (%)	13 885 (44.0%)	2820 (43.9%)	2574 (43.0%)	2640 (42.9%)	2543 (42.2%)	3308 (47.2%)
Men, n (%)	17 693 (56.0%)	3597 (56.1%)	3406 (57.0%)	3515 (57.1%)	3478 (57.8%)	3697 (52.8%)
Age*1, mean (SD)	49.0 (12.3)	49.4 (12.2)	47.8 (12.1)	48.1 (12.6)	48.4 (12.6)	50.8 (11.5)
BMI*2, mean (SD)	26.6 (4.79)	26.7 (4.75)	25.7 (4.43)	26.6 (4.95)	26.4 (4.71)	27.5 (4.89)

*1 In years; *2 in kg/m^2; BMI, body mass index; SD, standard deviation

Figure



Box plots for total brain volume by age decade and by sex
a) Raw data for total brain volume (cm^3). b) Residuals of total brain volume, corrected for height and weight.
Note that the oldest group includes only participants ranging in age from 70 to 74 years (light blue and light red).

Side effects, safety, and comfort

During the entire baseline study period, no severe adverse events were recorded. Four mild adverse events (0.013%) were reported, with occurrence of nausea/ vertigo/ vomiting in three cases and temporary tinnitus in one case.

Of the 2500 questionnaires on satisfaction, 2484 were completed and analyzed *(Table 2)*. Altogether, 98.5% of the participants were satisfied with the consenting procedure (82.3% very satisfied) and 99.5% of the participants were satisfied with the overall course of events at the MRI examination centers (83.8% very satisfied). The majority rated the duration of the MRI examination as "alright" (93.2%), while a minority of 5.9% rated the examination as "too long."

MRI image quality

On average, the radiologists rated the image quality as good in 9.8% of cases (range 3.0–18.7%) and as excellent in 89.0% (range 80.2–96.8%). In contrast, across all sequences, an average of only 1.2% (range 0.2–2.3%) of the image data acquired were rated as inadequate for post-processing. The automated image quality assessment also showed excellent results. Detailed information is provided in the *eSupplement*, which also contains an overview of the derived imaging parameters *(eSupplement, Table 1, eFigure)*.

Examination of total brain volume, white and gray matter volume, and cerebrospinal fluid volume from the T1w imaging data revealed highly consistent results across

Table 2

Results of the satisfaction survey conducted in connection with the baseline MRI examination at the five NAKO study centers at intervals of 6 months between fall 2016 and fall 2018 (100 questionnaires per site and time point)

	N	Not specified	Very satisfied	Satisfied	Partially satisfied	Dissatisfied	Very dissatisfied
Consenting procedure	2484	0.8%	82.3%	16.2%	0.2%	< 0.1%	0.4%
Overall procedure at MRI study center	2484	0.1%	83.8%	15.7%	0.3%	0.1%	< 0.1%
	N	Not specified	Too long		Alright	Too short	
Duration of MRI examination	2484	0.5%	5.9%		93.2%	0.4%	

MRI, Magnetic resonance imaging

Table 3

Means and standard deviations for the volumes of gray matter, white matter, cerebrospinal fluid, and total brain (cm^3) for the whole magnetic resonance imaging sample and separately for men and women*

	Whole sample					Men					Women				
Age group	N	GMV	WMV	CSF	TBV	N	GMV	WMV	CSF	TBV	N	GMV	WMV	CSF	TBV
Total	29 798	648.15 (62.95)	468.32 (58.28)	304.12 (62.20)	1143.92 (116.95)	16 647	679.57 (55.67)	495.84 (52.73)	327.03 (60.14)	1203.82 (102.06)	13 151	608.38 (47.17)	433.49 (44.78)	275.11 (51.80)	1068.10 (86.69)
20–29	3109	699.07 (63.45)	468.79 (58.09)	249.41 (44.15)	1195.67 (118.44)	185	732.92 (52.61)	496.18 (51.66)	267.55 (41.35)	1258.04 (99.43)	1324	653.42 (45.76)	431.86 (44.18)	224.95 (35.09)	1111.58 (85.44)
30–39	3553	677.67 (61.25)	477.81 (58.21)	266.94 (46.30)	1183.62 (116.32)	2102	709.93 (49.22)	504.64 (51.70)	286.70 (40.69)	1243.79 (95.78)	1451	630.94 (44.57)	438.95 (43.26)	238.33 (38.29)	1096.45 (83.66)
40–49	8780	653.04 (58.44)	475.94 (58.11)	293.45 (49.25)	1156.92 (113.90)	4930	685.70 (47.88)	504.35 (51.89)	313.91 (44.27)	1219.10 (95.32)	3850	611.23 (41.70)	439.55 (43.53)	267.24 (42.43)	1077.30 (81.62)
50–59	8240	636.61 (55.23)	469.65 (57.29)	316.35 (55.38)	1133.73 (109.71)	4526	665.60 (47.47)	496.84 (51.74)	341.61 (50.06)	1190.78 (94.77)	3714	601.28 (41.82)	436.52 (44.95)	285.55 (45.00)	1064.20 (83.43)
60–69	5704	614.37 (53.53)	450.65 (55.80)	350.12 (62.31)	1091.22 (105.98)	3061	642.79 (46.46)	477.30 (50.93)	382.10 (54.81)	1146.94 (92.69)	2643	581.46 (40.82)	419.79 (44.05)	313.07 (48.41)	1026.69 (80.83)
70–74	412	603.77 (49.57)	438.77 (55.52)	383.48 (66.28)	1067.72 (101.81)	243	624.45 (45.22)	459.33 (53.06)	413.91 (58.15)	1109.43 (94.48)	169	574.04 (39.47)	409.22 (44.68)	339.71 (51.09)	1007.74 (79.78)

* The overall mean values across all age groups (20–74 years) and the means for the individual decades
CSF, Cerebrospinal fluid volume; GMV, gray matter volume; TBV, total brain volume; WMV, white matter volume

all MRI study centers *(Table 3)*. Men showed slightly higher brain volumes than women (1203.81 ± 102.06 cm^3 vs. 1,068.10 ± 86.69 cm^3; *Figure a*), even after correction for body size and weight *(Figure b)*. Higher age was associated with lower total brain and gray matter volumes, while white matter volume remained constant and cerebrospinal fluid volume increased slightly *(eFigure)*. Age-related differences with regard to gray matter and cerebrospinal fluid were slightly greater in men than in women. Nevertheless, the associations were very similar across MR sites and were independent of biological sex.

Discussion

This article presents results of the analysis of quality indicators for the NAKO baseline MRI examination. The participation rate was exceptionally high and the dropout rate very low. Furthermore, the participants reported high levels of safety and comfort. Image quality was subjectively and objectively rated as good to excellent. Moreover, the brain volume findings were extremely consistent across all study centers. This lays the foundation for a qualitatively and quantitatively top-class image database and represents an excellent jumping-off point for epidemiological and radiological research using the NAKO MRI data.

The sample comprised a total of 31 578 women and men from five MRI study centers and 6 neighboring NAKO study centers, randomly selected from the regional resident registration offices, that supplied participants. The MRI participants represent only a subsample of the NAKO cohort, because MRI is a time-consuming and complex procedure that requires specific expertise and workflows. This corresponds to the approach taken in other large-scale population studies (6, 21, 22).

Those who participated in the NAKO MRI examination were middle-aged (mean age 49.0 ± 12.3 years) and more often male (56.0%), whereas the total NAKO sample had a slight preponderance of female participants (50.4%) (7). Possible explanations are that women perceive a greater risk of harm from complex imaging examinations (23) and/or are more averse to unknown scenarios (24). Furthermore, possible or actual pregnancy could also play a role. Similar observations on participation rates in population-based MRI studies have been made in KORA-MRI (6), the UK Biobank (4, 25), and other large clinical trials despite considerable efforts to increase the proportion of women among the participants (26).

The average BMI (26.6 ± 4.79 kg/m^2) and other major characteristics of the NAKO MRI subpopulation (including age and gender distribution) are also comparable with other larger cohorts. In the UK Biobank study, for instance, the mean BMI in the MRI sample was 26.6 ± 4.4 kg/m^2 (27). Therefore, our sample—although slightly different from the overall NAKO cohort (mean BMI 27.4 ± 4.4 kg/m^2 for men and 26.3 ± 5.5 kg/m^2 for women) (28)—may serve as a valid source for comparing or merging results of different cohort studies (29).

Notably, an extraordinary level of safety and comfort was achieved. Not a single severe adverse event was reported over the whole study period, and the prevalence of mild adverse events (e.g., nausea) was negligibly low. This was by no means unexpected, as in clinical scenarios a similarly safe environment can be assured by the radiology staff and the specific equipment (30). Ultimately, these conditions may also have contributed to the very low dropout rates.

Image quality was almost exclusively rated as good to excellent, and only a small proportion of data sets were judged unsuitable for image analysis. For the T2-weighted HASTE sequences this was 2.3%, opposed to only 0.2% for the T1-weighted MPRAGE sequences (see *eSupplement, Table 1*). In the NAKO MRI study, image quality was ensured by comprehensive quality management, including identical software and hardware as well as training, certification, and implementation of quality assurance procedures throughout the study period.

As a kind of proof of concept, we have conducted analyses of commonly examined imaging biomarkers (brain volumes), which replicate previously reported associations between increasing age and decreasing total brain and gray matter volumes (31). Furthermore, the known differences between the sexes, whereby men show higher volumes than women, were also observed in our data sets *(Figure a)*. The most powerful explanatory factor for these differences seems to be the greater height of men (32, 33). Correction of our data for height and weight considerably diminishes the differences in brain volumes between the sexes *(Figure b)*. Some of the remaining sex-specific differences in brain volumes may result from limitations of the statistical correction methods. However, cognitive function depends more on factors such as efficiency, connectivity, and specific regional volumes than on a larger total brain volume (34). These observations showed a high degree of similarity across all MR study centers, indicating high comparability among the sites *(eFigure)*.

In conclusion, the NAKO baseline MRI examination achieved an extremely high participation rate and provided a high level of participant safety and comfort throughout the study period. Among the 31 578 persons who participated in the baseline MRI examination, the rate of complete data sets was high and very good subjective and objective image quality was attained. The MRI database now provides an ideal source for complex image analysis projects and will make a decisive contribution to generation of novel insights into multiple disease entities in future research.

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The members of the NAKO Investigators Consortium acted as Collaborators (see *eBox 2*)

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Funding
This project was conducted with data (Application No. NAKO-796) from the German National Cohort (NAKO) (www.nako.de). The NAKO is funded by the Federal Ministry of Education and Research (BMBF) [project funding reference numbers: 01ER1301A/B/C, 01ER1511D, 01ER1801A/B/C/D and 01ER2301A/B/C], federal states of Germany and the Helmholtz Association, the participating universities and the institutes of the Leibniz Association.

Acknowledgments
We thank all participants who took part in the NAKO study and the staff of this research initiative.

Ethics
The NAKO Health Study was performed with the approval of the relevant ethics committees and is in accordance with national law and with the Declaration of Helsinki of 1975 (in the current, revised version).

Conflict of interest statement
FB holds shares in Siemens Healthineers. He receives financial support from Siemens, Philips, Sanofi, and Bayer.

KB is a member of the Editorial Board of Deutsches Ärzteblatt.

MF receives financial support from Siemens, Philips, Boehringer, and Sanofi.

HUK has received financial support from Siemens and Philips.

The remaining authors declare that no conflict of interest exists.

Manuscript received on 21 December 2023, revised version accepted on 15 July 2024.

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Cite this as:
Bamberg F, Schlett CL, Caspers S, Ringhof S, Günther M, Hirsch JG, Rüdebusch J, Miklánková P, Bittner N, Jockwitz C, Forsting M, Hosten N, Kaaks R, Kauczor HU, Kroenke T, Niendorf T, Peters A, Pischon T, Stang A, Berger K, Völzke H, NAKO Investigators Consortium: Baseline MRI examination in the NAKO Health Study—findings on feasibility, participation and dropout rates, comfort, and image quality. Dtsch Arztebl Int 2024; 121: 587–93. DOI: 10.3238/arztebl.m2024.0151

Supplementary material
eFigure, eBoxes:
www.aerzteblatt-international.de/m2024.0151

Supplementary material to accompany the article:

Baseline MRI Examination in the NAKO Health Study

Findings on Feasibility, Participation and Dropout Rates, Comfort, and Image Quality

by Fabian Bamberg, Christopher L. Schlett, [...]* Klaus Berger, and Henry Völzke

Dtsch Arztebl Int 2024; 121: 587–93. DOI: 10.3238/arztebl.m2024.0151

eBox 1

Exclusion criteria for participation in whole-body MRI examination as part of the NAKO Health Study

- Cardiac pacemaker or intracardiac defibrillator
- Medical foreign bodies not considered safe for 3-T MRI, e.g., cerebral aneurysm clip, cochlear implant, insulin pump, prosthetic cardiac valve
- Other orthopedic implants not considered safe for 3-T MRI, including screws, plates, and joint prostheses, and/or metallic foreign bodies such as shrapnel or bullets
- Surgical procedures in the head, abdomen, or back within 3 months prior to the MRI examination
- Non-removable metallic body art
- Tattoos (larger than the size of the participant's palm or applied more than 20 years earlier) or make-up not considered safe for 3-T MRI (permanent/glossy make-up)
- A possible ferromagnetic intrauterine pessary (e.g., one containing copper)
- (Possible) pregnancy
- Claustrophobia
- Deafness
- Inability to hold breath (for approximately 10 seconds) or lie supine (for approximately 1 hour)
- No consent to be informed of potential incidental findings

eBox 2

The members of the NAKO Investigators Consortium (collaborators)

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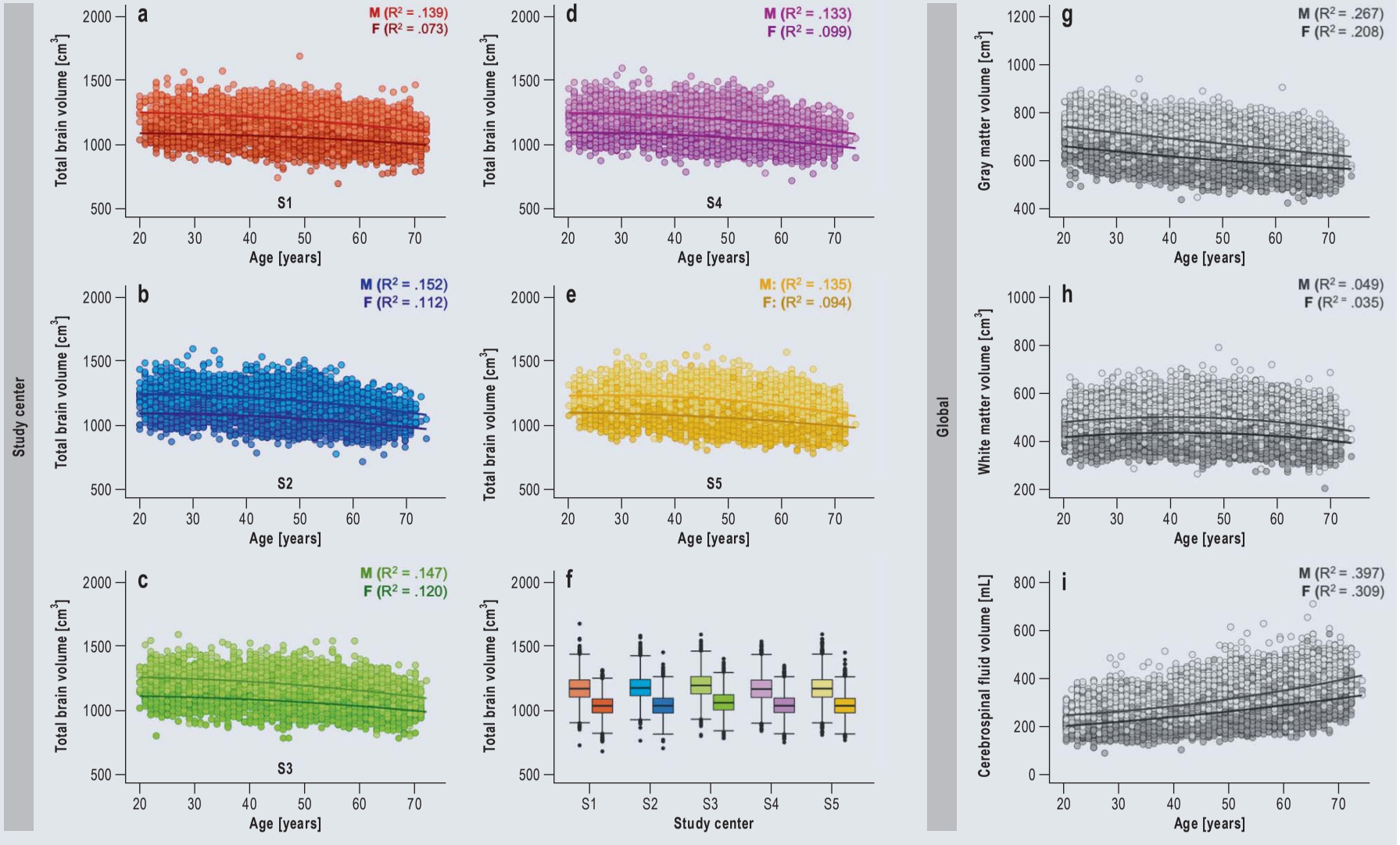
- Prof. Dr. med. Sabine Weckbach, Department of Diagnostic and Interventional Radiology, University Hospital Heidelberg, Germany
- Dr. rer nat. Nicole Werner, Institute for Community Medicine, University Medicine Greifswald, Germany

eFigure



Brain morphological image quality examination

a–f) Age-related differences in total brain volume per MRI study center (Augsburg = S1 = red [n = 6074], Berlin = S2 = blue [n = 5708], Essen = S3 = green [n = 5743], Mannheim = S4 = pink [n = 5609], Neubrandenburg = S5 = yellow [n = 6664]); lighter colors = men, darker colors = women. f) Box plots showing the average total brain volume for the two sexes separately (lighter colors = men [n = 16 647], darker colors = women [n = 13 151]).
g–i) Age-related differences in gray matter volume, white matter volume, and cerebrospinal fluid volume for the two sexes separately (light gray = men, dark gray = women).

Supplementary material

MR IMAGE QUALITY

Methods

MR image quality was assessed by certified radiologists. Visual quality was rated on a three-tier scale according to predefined quality criteria. For this purpose, images obtained for each protocol series were classified into either one of the following categories: 1) image quality excellent, no presence of impairing artifacts, images appropriate for data post-processing; 2) image quality good to very good with presence of artifacts resulting in limited image quality, but images appropriate for data post-processing; 3) poor to fair image quality due to artifacts / insufficient coverage, generally not appropriate for image post-processing.

A fully automated data management workflow preceded the radiologists' reading for incidental findings and the review of image quality. This included automated registering of participants (pseudonomized) at the MRI scanner using a DICOM Modality Worklist server fed by centralized NAKO participant information. Continuous data transfer in sync with data acquisition was secured via VPN-secured DICOM transfer protocol to a centralized data base. Subsequent automated quality assessment (QA) covered methodological and technical aspects, as well as deviations from the MRI study protocol (protocol order changes and repetitions, parameter changes, missing sequences). Furthermore, a series of image-based quality measures were derived (15), including i.e. common values (object position, signal-to-noise-ratio, sharpness, universal image quality index), artifact specific parameters (structured noise, Nyquist ghosting), and protocol specific parameters (intensity drift, motion detection in fMRI time series) (16, 17). All image DICOM metadata and assessed QA data were stored to an ElasticSearch database for further analyses.

Statistics

MR image quality across all MR sites was compared using QA indices, violin and box plots, together with median, mean and 95% confidence intervals. Results are summarized in an intuitive graph visualizing data distribution and describing the short-term characteristics. Additionally, time trends were assessed with LOESS-smoothed plots.

Short-term and long-term stability as well as consistency across MR centers were evaluated continuously during a three-months-period using violin plots. Mean values, 95% confidence intervals and 25%-75% percentile ranges were used to assess overall image quality for each MRI site as well as for site-to-site comparisons. Further, LOESS curves and their 95% confidence intervals (e1) were applied to describe the development over time for all estimated quality indices and for all sequence protocols, to be able to identify slowly developing trends, site-to-site differences and sudden onsets of

technical failures. Outliers were defined according to several criteria for outlier detection (e2) to better detect exams with severe artifacts, subject motion, mispositioning and technical failures.

We used SAS (Version 9.5) and NIST DataPlot (National Institute of Standards and Technology, Gaithersburg, MD, USA) for statistical analyses.

Results

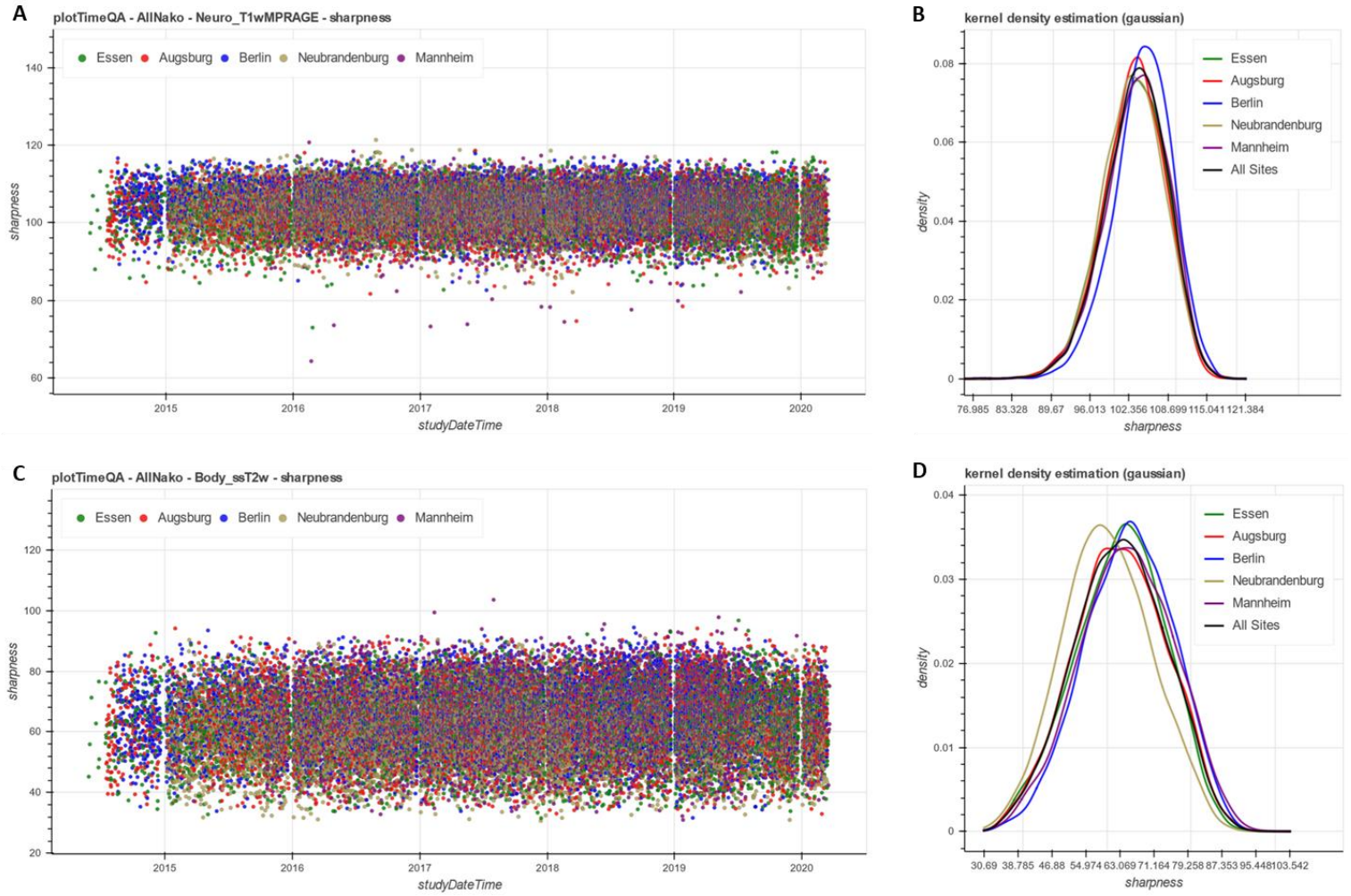
On average, the image quality was classified as appropriate for image analysis in more than 97%. Similarly, the automated image quality assessment demonstrated on average excellent results, with respect to the multi-center aspect, as well as to the longitudinal evaluation. Supplementary Table 1 illustrates the automated image quality pooled over all imaging centers.

With respect to the individual Quality Assessment (QA) scores per subject, per protocol, and per QA index, the long-term trend over five years indicated very stable and consistent results across the course and MRI sites. Supplementary Figure 1a exemplarily depicts the QA index "image sharpness" with an overall mean of 103.5 (SD 5.0). The distribution plots for each MRI site (Supplementary Figure 1b) reveal a high homogeneity between the sites. In comparison, for the T2w HASTE (lung and abdomen coverage) QA value distributions are wider (sharpness 63.3 ± 10.9) and some systematic value shifts between MRI sites occurred, mostly due to much stronger sensitivity to motion artifacts, local magnetic field shimming, etc. The T2w HASTE sequence represents the lower end of quality range. Detailed information on the QA indices sharpness, universal image quality, and signal-to-noise-ratio (SNR) for all protocols is also provided in Supplementary Table 1. Individual QA values per subject, separately for each MRI site, are cumulated and reported in forms of violin plots in Supplementary Figure 2.

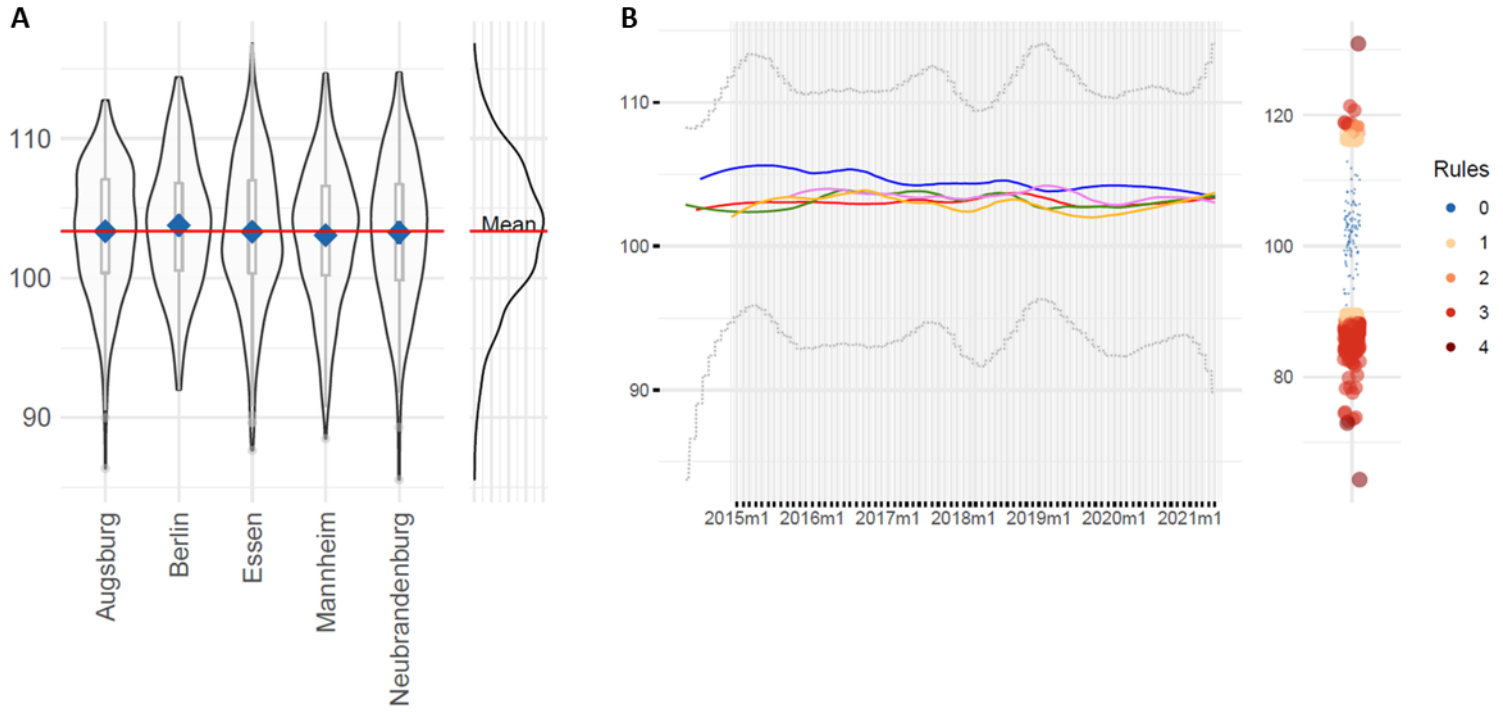
Supplement, Table 1: Subjective visual and automated image quality during the NAKO baseline examination stratified by acquired MR sequence.
Visual quality assessment (Visual QA) was measured on a 3-point Likert-scale, ranging from "poor" (image quality not appropriate for post-processing due to strong artifacts or inadequate coverage), to "excellent" (image quality excellent, no presence of impairing artifacts, images appropriate for data post-processing). Automated image-based QA indices universal image quality index (Univ. IQI) and Sharpness were evaluated for all sequences. Signal-to-Noise-Ratio (SNR) is provided for sequences pertaining to the brain with adequate background noise only.

MR sequences	**Visual QA**			**Automated image quality**		
	Excellent	**Good**	**Poor**	**Univ IQI**	**Sharpness**	**SNR**
T1 MPRAGE (S05)	29,711 (96.8 %)	915 (3.0 %)	53 (0.2 %)	0.53 ± 0.02	103.5 ± 5.0	42.1 ± 6.4
FLAIR 2D (S06)	26,904 (87.9 %)	3624 (11.8 %)	88 (0.3 %)	0.40 ± 0.02	71.6 ± 3.70	33.3 ± 5.5
Resting State (S07)	-	-	-	0.47 ± 0.02	94.0 ± 2.2	115.7 ± 11.7
PD_FS_Hip (S03)	24,682 (80.2 %)	5,769 (18.7 %)	330 (1.1 %)	0.30 ± 0.03	51.5 ± 3.4	-
T2w_Spine (S08)	29,033 (95.2 %)	1,303 (4.3 %)	153 (0.5 %)	0.36 ± 0.03	68.1 ± 4.5	-
T1wVibe_Dixon (S09)	27,696 (91.1 %)	2,076 (6.8 %)	627 (2.1 %)	0.35 ± 0.04	73.6 ± 5.5	-
T2w_HASTE (S10)	25,112 (82.7 %)	4,551 (15.0 %)	627 (2.3 %)	0.21 ± 0.05	63.3 ± 10.9	-
ME_Vibe_FatQ (S11)	-	-	-	0.24 ± 0.02	59.3 ± 7.4	-
MRA_Thorax (S12)	28,357 (93.7 %)	1,765 (5.8 %)	157 (0.5 %)	0.38 ± 0.03	59.0 ± 4.1	-
CINE_LAX (S14)	25,555 (85.1 %)	3,905 (13.0 %)	571 (1.9 %)	0.29 ± 0.04	47.0 ± 3.9	-
CINE_SAX (S15)	26,438 (88.3 %)	3,041 (10.2 %)	478 (1.6 %)	0.31 ± 0.03	50.0 ± 4.0	-
MOLLI_T1 (S16)	-	-	-	0.28 ± 0.04	43.9 ± 4.9	-

QA = quality assessment; Univ. IQI = universal image quality index; SNR: signal-to-noise-ratio. T1 MPRAGE: 3D T1-weighted gradient-echo; FLAIR 2D: 2D T2-weighted fluid attenuated inversion recovery TSE; Resting State: 2D echo-planar BOLD acquisition; PD_FS_Hip: 3D PD-weighted SPACE with fat saturation; T2w_Spine: 2D T2-weighted TSE (whole spine coverage); T1w_VIBE_Dixon: 3D T1w fat suppressed gradient echo with two-point Dixon fat/water separation; T2w_HASTE: 2D T2-weighted echo-planar fast spin echo; ME_VIBE_FatQ: multiecho 3D T1w VIBE with T2*-corrected Dixon fat/water separation; MRA_Thorax: 3D MR angiography with thoracic coverage using an inflow inversion recovery SPACE; CINE_LAX: 2D cine steady-state free precession in long-axis orientation (single slice); CINE_SAX: 2D cine steady-state free precession in short-axis orientation (multiple slices); MOLLI_T1: single slice myocardial T1-mapping using a modified Look-Locker inversion recovery.



Supplement, Figure 1: A) Single-value quality assurance plots over time and (B) quality assurance value distributions for each MR site with respect to the QA index "Sharpness" (mean±SD = 103.5 ± 5.0) for sequence T1w MPRAGE of the brain. Similar information over time (C) and MR site (D) for the sequence T2w HASTE (body), sharpness = 63.3 ± 10.9, revealing a wider distribution of QA values and some systematic shifts between different MR sites.



Supplement, Figure 2: Image-based automated quality assessment including several quality indices (signal-to-noise ratio, sharpness, universal image quality, structured noise and Nyquist-ghost correlation coefficients, signal intensity drift, subject motion). (A) Violine plots (with diamonds representing mean values) for the quality index "sharpness" of the MR sequence T1w MPRAGE across all MR imaging sites is provided, indicating an excellent multi-center consistency. (B) Similarly, LOESS plots depicting time-trends of quality related indices within sites (red = Augsburg, blue = Berlin, green = Essen, pink = Mannheim, yellow = Neubrandenburg; grey boundaries indicate the 99% confidence interval) allowing to identify outlier per rule with impaired image quality, i.e. incorrect table position, severe motion, technical failures) on a single data point level.

Discussion

Despite the image quality was rated very high, which was confirmed by objective, automated assessment of image quality, there was a small portion (2.3%) of T2-weighted HASTE sequences which were rated not suitable for image analysis (as opposed to only 0.2% in the T1-weighted MPRAGE sequences). In fact, it is known that T2-weighted HASTE is prone to breathing/motion artifacts or imperfect magnetic field shimming, due to longer signal read-outs, which may exceed the duration of the breath-hold acquisitions. This shortcoming motivates the development and clinical translation of novel, rapid spin-echo based MRI techniques, such as Deep Learning-Accelerated acquisition techniques with Variable Refocusing Flip Angles are currently being evaluated (e3). Another direction to enhancing images primarily rated not feasible for high-quality image post-processing using Deep Learning (e4). Furthermore, decreased image quality is leading to increased scan time due to repeating of MR protocols leading to increased costs and decreases subjects' comfort and satisfaction (15). Achieving a high level of quality is of critical relevance for the NAKO study, as all subsequent image analysis clearly depends on well analyzable images. The needed high image quality can be best ensured through extensive quality management activities including identical soft- and hardware and training / certification / quality assurance throughout the study period. The obtained quality also justifies the tremendous effort of all study staff and the significance of public funding allocated to the MR imaging component of the NAKO. In fact, the validity of all subsequently image-derived parameters of participant's characteristics (imaging biomarkers) heavily depends on the input quality of imaging information provided through the repository of the baseline MRI examination (e5).

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