

# Cortical thinning in former professional soccer players

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**Abstract** Soccer is the most popular sport in the world. Soccer players are at high risk for repetitive subconcussive head impact when heading the ball. Whether this leads to long-term alterations of the brain's structure associated with cognitive decline remains unknown. The aim of this study was to evaluate cortical thickness in former professional soccer players using high-resolution structural MR imaging. Fifteen former male professional soccer players (mean age 49.3 [SD 5.1] years) underwent high-resolution structural 3 T MR imaging, as well as cognitive testing. Fifteen male, age-matched former professional non-contact sport athletes (mean age 49.6 [SD 6.4] years) served as controls. Group analyses of cortical thickness were performed using voxel-based statistics. Soccer players demonstrated greater cortical thinning with increasing age compared to controls in the right inferolateral-parietal, temporal, and occipital cortex. Cortical thinning was associated with lower cognitive performance as well as with estimated exposure to repetitive subconcussive head impact. Neurocognitive evaluation revealed decreased memory per-

formance in the soccer players compared to controls. The association of cortical thinning and decreased cognitive performance, as well as exposure to repetitive subconcussive head impact, further supports the hypothesis that repetitive subconcussive head impact may play a role in early cognitive decline in soccer players. Future studies are needed to elucidate the time course of changes in cortical thickness as well as their association with impaired cognitive function and possible underlying neurodegenerative process.

**Keywords** Repetitive subconcussive head impact · Soccer · Cortical thickness · Aging · Traumatic brain injury

## Abbreviations

BIS	Barrett Impulsivity Score
BESS	Balance error scoring system
ROCF	Rey osterrieth complex figure
RSHI	Repetitive subconcussive head impact

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TMT A Trailmaking Test A  
TMT B Trailmaking Test B

## Background

Soccer is the most popular and fastest growing sport in the world, with more than 250 million active players worldwide. Head impact in soccer can be a result of a single blow from the ball, of striking the ground, or of a collision with another player or with the goalpost (Boden et al. 1998). More common, however, are subclinical or subconcussive head impacts that do not result in acute symptoms (Bailes et al. 2013). Frequently heading a soccer ball has been discussed as a source of subconcussive head impact in soccer (Koerte et al. 2012, 2015b; Lipton and Kim 2013; Jordan et al. 1996). On average, professional soccer players perform 6–12 headings per game, resulting in thousands of headings over a player's career (Ekblom 1986; Rutherford et al. 2009; Straume-Naesheim et al. 2005; Tysvaer and Storli 1981). Because there is often no clinical manifestation, subconcussive head impacts are often thought to be harmless. Recent evidence suggests, however, a link between heading the ball and reduced cognitive performance immediately after training (Zhang et al. 2013). Additionally, exposure to repetitive subconcussive head impact may lead to alterations in the brain's white matter microstructure in young soccer players (Koerte et al. 2012; Lipton and Kim 2013). We also recently showed that repetitive subconcussive head impacts are associated with changes in brain chemistry in former professional soccer players (Koerte et al. 2015a). However, whether or not repetitive heading the ball has the potential to elicit long-term alterations of the brain's structure, such as cortical thickness, associated with cognitive decline remains unknown (Rieder and Jansen 2011).

Impaired memory performance has been recently associated with accelerated decrease in cortical thickness in former contact-sports athletes such as American football players (Tremblay et al. 2013). Although alterations in gray matter are also likely to play a role in cognitive decline in soccer players, to date, such alterations have not been systematically investigated. This is the first study to evaluate the association between cortical thickness and estimated exposure to repetitive subconcussive head impact, as well as to cognitive performance in former professional soccer players compared to age-matched non-contact sport athletes.

## Methods

### Participants

All soccer players from two senior training groups of an elite level soccer club in Germany were approached to participate in the study. Inclusion criteria were participation in at least one play

season of professional soccer, being male, age between 40 and 65 years, and right-handedness. Exclusion criteria were history of moderate or severe traumatic brain injury, neurological disorder, or psychiatric illness. Fifteen out of 16 interested players met the study criteria and were included in the study cohort. One interested player was excluded from participation due to a history of severe traumatic brain injury unrelated to contact-sports. The local ethics committee approved the study and written informed consent was obtained from each participant.

The study cohort consisted of 15 former professional soccer players who participated in at least one professional play season (mean 4.7 [SD 3.6] years). In addition, soccer players were still actively participating in soccer on a recreational level up to twice a week at the time of the study. All players (mean age 49.3 [SD 5.1] years) were trained in soccer since childhood. Two of the soccer players had a history of mild traumatic brain injury during childhood due to a vehicle accident. A comparison cohort of 15 athletes (all male, mean age 49.6 [SD 6.4] years) was recruited from competitive athletic clubs, and matched on age-, and handedness. These subjects were former competitive athletes and were still actively participating in non-contact sports at the time of the study. Non-contact sports with minimal exposure to repetitive brain trauma included running ( $n = 6$ ), table tennis ( $n = 7$ ), and ballroom dancing ( $n = 2$ ). 11 of the 15 athletes and 14 of 15 controls were previously reported in an earlier publication (Koerte et al. 2015a) however using a different imaging modality (magnetic resonance spectroscopy).

### Clinical information, neuropsychological evaluation, and balance test

A semi-structured interview was performed to acquire detailed information about training habits and lifestyle, including *number of headings performed per week during the last year*, and *position in the field*. Players were asked how many headers they performed per week during the past 12 months prior to the study. The rationale behind asking for this time period is that self-report is known to be less reliable when asking about a time period that is further in the past. To obtain a lifetime-estimate of headers, the number of headers per week during the last year was multiplied by the total years of organized training in soccer.

All study participants underwent evaluation of cognitive, behavioral, and motor functioning by an examiner who was blinded to the athlete's sport. Study participants were asked to not talk about their respective sport to the examiner conducting the neuropsychological tests in order to ensure the blind. Tests included: Trailmaking Test (TMT) parts A and B, Rey Osterrieth Complex Figure (ROCF), Barrett Impulsivity Score (BIS), and the Balance Error Scoring System (BESS). TMT parts A and B were performed to quantify the athlete's psychomotor speed, visual search, and mental

flexibility (Bowie and Harvey 2006). The ROCF test is a measure of visuoconstructional ability and visual memory (Shin et al. 2006) requiring the subject to reproduce a line drawn figure while looking at it (copy condition), and then again after a delay of five minutes (short delay recall condition), and after a delay of 30 min (long delay recall condition). The BIS, a 30-item questionnaire describing common impulsive or non-impulsive behaviors and preferences was used to quantify the athlete's impulsivity (Patton et al. 1995). The BESS is a commonly used measure of balance, consisting of 3 different positions (double leg, single leg, tandem) on two different surfaces (foam and firm) over 20 s, respectively (Bell et al. 2011).

### MR imaging data acquisition

Data acquisition was performed in a supine position on a single 3 T MR scanner (Magnetom Verio, Siemens Healthcare, Erlangen, Germany) with a 32-channel head coil array. The scanning protocol included the following structural sequences: T1-weighted 3D magnetization prepared rapid-acquisition gradient echo (MP-RAGE) acquired in a sagittal orientation and motion insensitive 3D T2-weighted BLADE sequence acquired in a transversal orientation. Imaging parameters were as follows: MP-RAGE: TR = 1800 ms, TE = 3.06 ms, FOV = 256 mm, voxel size =  $1 \times 1 \times 1 \text{ mm}^3$ , iPAT, acceleration factor 2; 3D T2-weighted BLADE sequence: TR = 3000 ms, TE = 400 ms, FOV = 250 mm, voxel size =  $1 \times 1 \times 1 \text{ mm}^3$ , slices = 160, iPAT, acceleration factor 2.

### Cortical thickness analysis

MRI data sets were examined for image quality. The T1-weighted images were transformed from DICOM to NRRD file format by creating an nhdr header file for each subject. Scans were again subject to quality and orientation control. Cortical thickness analysis was then performed using FreeSurfer version 5.3 (Athinoula A. Martinos Center for Biomedical Imaging, Charlestown, MA, USA). The fully automated cortical reconstruction process was applied. A detailed description of this process is available on the FreeSurfer website (<http://ftp.nmr.mgh.harvard.edu/fswiki/recon-all>). Briefly, the images were aligned to a common atlas and the grayscale intensity was normalized and corrected for inhomogeneity of the magnetic field. All voxels were labeled as gray matter, white matter, or cerebral spinal fluid and the gray matter surface (pial) and the white matter surface were created. Cortical thickness is defined as the distance between the surface of the gray matter and the boundary between gray and white matter at each point on the cortical mantle. This method is sufficiently sensitive to detect differences at the sub-millimeter level between groups. For improved contrast, noise ratio cortical smoothing was applied,

which averages information from nearby voxels. The threshold was set to the default setting of 15 mm full width at half maximum.

### Statistics

Between-group differences in measures of cognitive, behavioral, and motor functioning were examined using independent sample T-tests. Cognitive and behavioral measures were correlated with lifetime-estimate of heading using Spearman Rho. Group comparison of cortical thickness with age as a covariate was performed using the qdec tool in FreeSurfer 5.3. The effect of *life-time estimate of headings* on cortical thickness was tested within the soccer cohort, with age included as nuisance factor. A z-distribution Monte Carlo simulation was then applied to correct for multiple comparisons. For all analyses a significance level was set at  $\alpha = 0.05$  (two-sided). GraphPad Prism 6 (GraphPad Software, La Jolla, CA, USA) was used to visualize the data.

## Results

### Clinical information and cognitive evaluation

The mean age when organized soccer training started was 9.5 [SD 4.9] years. The number of headers performed per week over the past year ranged between 1 and 70 (mean 32.9 [22.5]). On average this translates to 10 to 16 headers per game and per training session. The athletes played in the following positions: defense ( $n = 3$ ), midfield offensive ( $n = 8$ ), midfield defensive ( $n = 3$ ), and goalkeeper ( $n = 1$ ). The soccer and control group did not differ regarding body mass index (BMI) (mean 25.3 [SD 1.7] versus 24.2 [2.2],  $p = 0.14$ ).

All soccer players and controls tested within the normal range for age for TMT parts A and B, ROCF test, BIS, and BESS. However, there was a significant difference in memory performance using the ROCF. Soccer players performed worse on the long delay recall condition (mean T score 47.7 [14.7] versus 56.9 [8.8],  $p = 0.04$ ). There were no other significant group differences on ROCF copy condition and short delay recall condition, TMT, BIS, or BESS. Results are listed in Table 1. No significant correlations were found between cognitive or behavioral measures with lifetime-estimate of headings.

### Cortical thickness

Group comparison with age as a covariate revealed a large cluster with significant differences observed for the interaction of group and age that involved the temporal, parietal, and occipital lobes, bilaterally (Fig. 1). Cortical thickness within the clusters showed a significantly greater decrease with age ( $p < 0.05$ ; corrected for multiple comparison) in the soccer

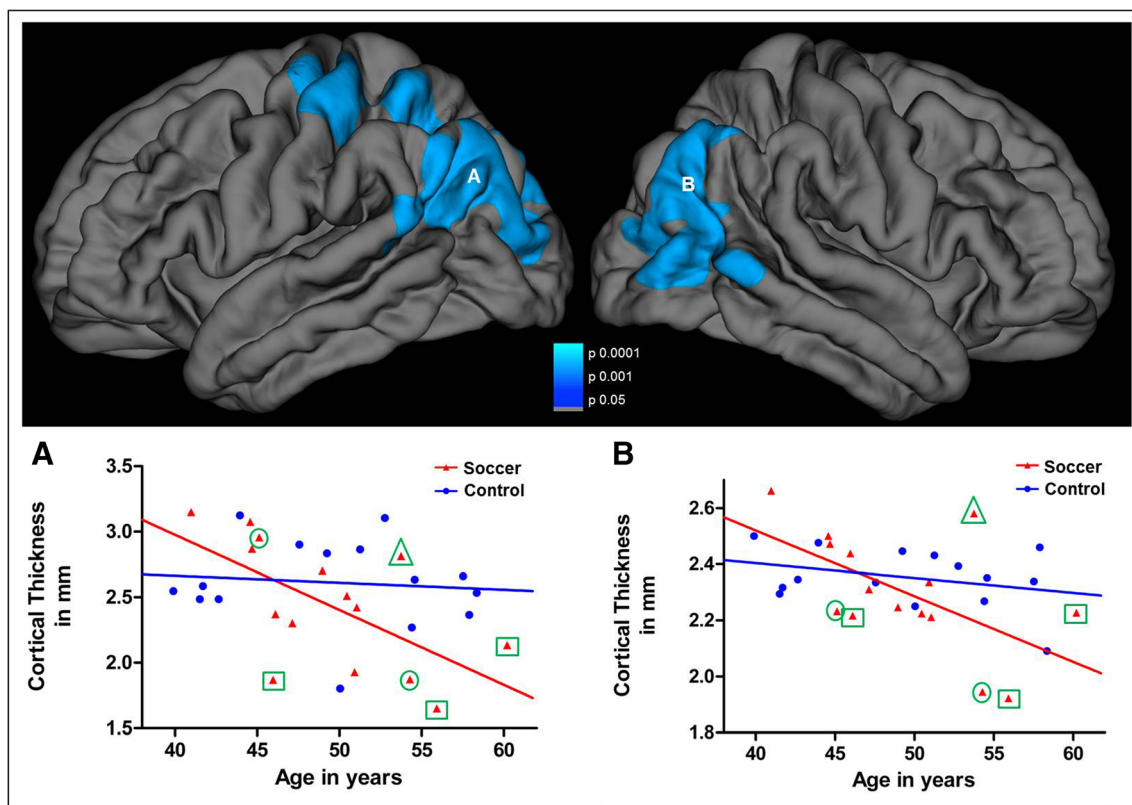
**Table 1** Results of the neuropsychological and neurological evaluation

		Soccer players	Athlete controls	<i>p</i> -value
		<b>N = 15</b>	<b>N = 15</b>	
<b>ROCF</b>	<b>Copy raw score</b>	34.4 (2.5)	34.8 (2.5)	0.66
	<b>Short delay recall T-score</b>	48.9 (10.9)	54.9 (7.6)	0.09
	<b>Long delay recall T-score</b>	47.7 (14.7)	56.9 (8.8)	<b>0.04</b>
<b>TMT A</b>	<b>Score</b>	103.9 (5.1)	102.6 (5.9)	0.54
<b>TMT B</b>	<b>Score</b>	108.5 (4.7)	109.9 (4.8)	0.45
<b>BIS</b>	<b>Attentional impulsiveness</b>	22.0 (3.9)	21.4 (4.6)	0.86
	<b>Motor impulsiveness</b>	22.1 (4.6)	20.2 (3.2)	0.24
	<b>Nonplanning impulsiveness</b>	21.5 (4.8)	20.4 (3.9)	0.85
	<b>Total score</b>	65.5 (11.5)	62.9 (10.4)	0.57
<b>BESS</b>	<b>Total score</b>	17.4 (7.1)	19.0 (7.6)	0.56

Note that the delayed recall condition of the Rey-Osterrieth complex Figure (ROCF) test revealed a significant difference between the two groups where soccer players performed worse than athlete controls. TMT A and B (Trailmaking Test A and B), BIS (Barett Impulsiveness Scale), BESS (Balance Error Scoring System). All results are given as mean scores (SD). *P*-values as obtained using two-sided student *t*-test

players compared to the control group (Fig. 1). There were no cortical regions (i.e., significant clusters) with greater decline in cortical thickness in the control group.

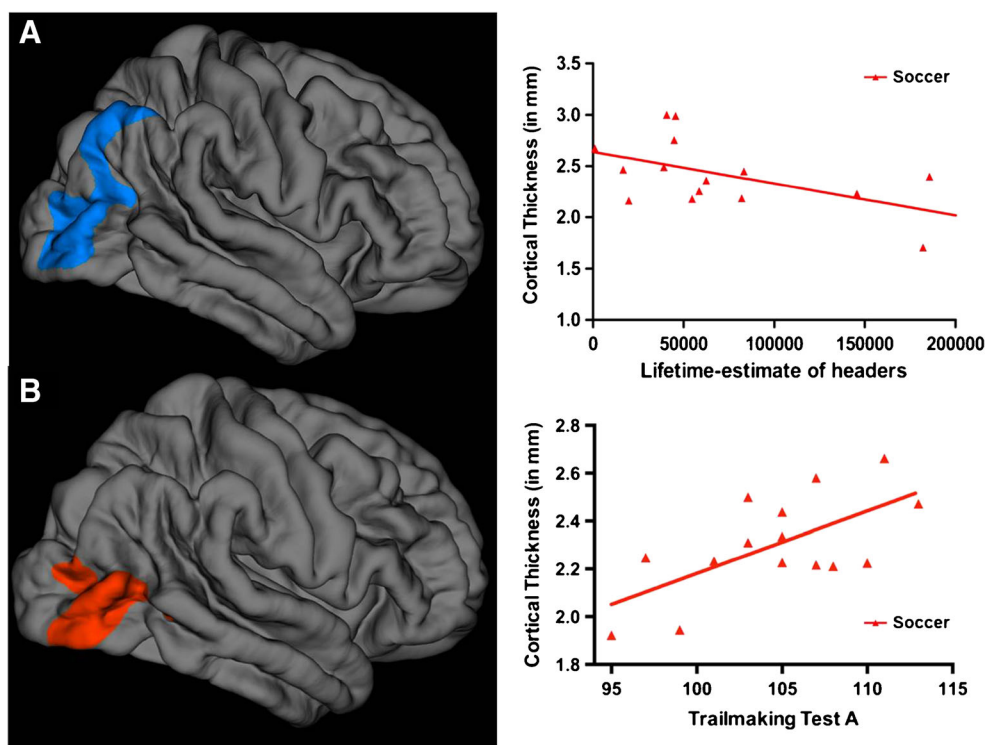
Within the soccer players, *lifetime-estimate of headings* significantly correlated with cortical thickness in a cluster that involved the right hemisphere parietal and occipital lobes (Fig. 2a).



**Fig. 1** Greater decrease in cortical thickness in former professional soccer players. Areas displayed in blue represent the two clusters with significant group  $\times$  age interaction with greater decrease in cortical thickness in former professional soccer players compared to non-contact athlete controls. The scatter plots display average cortical thickness for each individual in cluster “A” (left frontal, posterior parietal, occipital, and temporal cortex) and cluster “B” (right posterior

parietal, occipital, and temporal). Note the circled soccer players reported a history of mild traumatic brain injury while the ones highlighted with a square are those with the highest life-time estimate of headings. The goalkeeper is highlighted with a triangle. *P*-value thresholded at  $p < 0.05$  after correction for multiple comparisons using z-Monte Carlo simulation and Gaussian smoothing





**Fig. 2** **a** Correlation between cortical thickness and exposure to subconcussive head impact. Area displayed in blue represents the clusters with significant negative correlation between cortical thickness and exposure to subconcussive head impact within the soccer group. The scatter plot displays the average cortical thickness and life-time estimate of headers of each individual. **b** Correlation between cortical thickness and cognitive processing speed. Area displayed in orange represents the

clusters with significant positive correlation between cortical thickness and Trailmaking test A (TMT A) results within the soccer group. The scatter plot displays the average cortical thickness and TMT A standard score of each individual. The higher the score the better the performance (a score between 90 and 110 is considered normal). *P*-value thresholded at  $p < 0.05$  after correction for multiple comparisons using z-Monte Carlo simulation and Gaussian smoothing

Interestingly, there was an overlap between the cluster with a significant correlation between *life-time estimate of headings* and the cluster with age  $\times$  group interaction extending over the right inferolateral-parietal, temporal, and occipital cortex (Figs. 1 and 2a). The goalkeeper with low exposure to repetitive brain trauma while heading the ball was among those with the highest cortical thickness. The two soccer players with a history of mild traumatic brain injury were among those with the lowest cortical thickness in their respective age group.

TMT A positively correlated with cortical thickness in a cluster located in the right inferolateral-parietal cortex (Fig. 2b). There was again overlap between the previously mentioned cluster with a significant correlation between *life-time estimate of headings* and the cluster with age  $\times$  group interaction (Figs. 1 and 2b).

## Discussion

This study reports significantly greater cortical thinning with increasing age in former professional soccer players compared to age- and gender-matched athlete controls. Cortical thinning in soccer players was also associated with estimated exposure

to repetitive subconcussive head impact, slower cognitive processing speed, and decreased visual memory performance.

As expected, a decline in cortical thickness with age was found in both groups, as cortical thickness has been shown to decrease with age in the normal population (Sowell et al. 2007, Storsve et al. 2014, Fjell et al. 2009, Salat et al. 2004). The decline in cortical thickness in the control group was, nonetheless, well within the reported decline in cortical thickness observed with age (Sowell et al. 2007; Storsve et al. 2014; Salat et al. 2004). Of note, recently, a greater cortical thinning with age has been observed in individuals with a history of concussion (Tremblay et al. 2013). The two athletes with a history of concussion were among those with the thinnest cortex in their respective age group (Fig. 1). When excluding the two players with history of mild TBI, the cluster on the right hemisphere with significant age  $\times$  group interaction remained of similar size and within the same location, suggesting that these two players did not drive the results. Most importantly, the majority of soccer players in our study did not have a history of concussion. Nevertheless, the soccer group showed a greater cortical thinning with age, which was most pronounced in the bilateral parieto-occipital region, a brain region known to play a role in visuospatial functioning, visual working memory, and

attention. Those with the highest exposure to repetitive subconcussive head impact showed the thinnest cortex, suggesting a cumulative effect of subconcussive brain trauma. This is in line with our previous work demonstrating alterations of the white matter microarchitecture in younger professional soccer players without a history of concussion (Koerte et al. 2012).

Further, within the soccer group, cortical thinning in the right posterior parietal and occipital region was associated with estimated exposure to repetitive subconcussive head impact. There was also an overlap between this region and the cluster with group  $\times$  age interaction (Fig. 1), indicating that the group differences observed were a result of the difference in exposure to repetitive subconcussive head impact. Interestingly, and as noted previously, the goalkeeper with the least exposure to repetitive blows to his head was among those with the highest value for cortical thickness, suggesting a dose response relationship (Fig. 1). Additionally, a thicker cortex in the right inferolateral parietal region correlated with better performance in TMT A. Again, there was an overlap with the cluster with significant age  $\times$  group interaction, as well as with the cluster with a significant correlation between cortical thickness and estimated exposure to repetitive subconcussive head impact, thus tying the structural findings to both cognitive performance and estimated exposure to repetitive subconcussive head impact.

Even in this small cohort, soccer players demonstrated reduced performance in a visual memory task compared to controls, although findings were in the normal range for both groups. This finding may be an early indication of cognitive deficits that have been reported in this population later in life.

Limitations of this study include the small sample size and the fact that the information pertaining to history of subconcussion and concussion was based on the athlete's self-report. Thus the calculation of lifetime-estimate of headers provides only a rough estimate of the true exposure to repetitive subconcussive head impact. Moreover, information about number of headers does not take into account the forces that apply while heading the ball or the frequency of heading the ball during professional play compared to post-professional recreational play. Additionally, besides heading the ball, head injuries in soccer can also be a result of a single blow from the ball, of striking the ground, or of a collision with another player or the goalpost (Boden et al. 1998). Although the former professional soccer players were matched on age and gender with athletes of non-contact sports, other factors such as differences in diet and even life-style may play a role. Future studies need to include a larger sample, as well as more detailed information on education and socioeconomic background. In addition, more objective measures of frequency and forces that occur during exposure to repetitive subconcussive head impact are needed to evaluate further the effect of repetitive head impacts on cortical thickness. Evidence of neuroinflammation found in a previous study (Koerte et al. 2015a) may provide one potential

explanation for the underlying cause for cortical thinning, however, further neuroanatomical and possibly neuropathological studies are needed to address the cellular underpinnings of cortical thinning in athletes participating in contact-sports.

## Conclusion

In this small cohort of former professional soccer players, we observed greater cortical thinning with age than was observed in non-contact sport athletes. Additionally, the greater the estimated exposure to repetitive subconcussive head impact the soccer players experienced during their career, the thinner their cortex, and the thinner their cortex the lower their cognitive processing speed. This study also reports normal visual memory performance in soccer players, which was, however, decreased compared to non-contact athlete controls. These findings suggest that repetitive subconcussive head impacts may play a role in age-related cortical thinning that may lead to early cognitive decline in soccer players. We advocate for future longitudinal studies on larger cohorts to elucidate the time course of cortical thinning and its association with possible neurodegenerative disease.

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**Conflict of interest** All authors declare that they have no conflict of interest.

**Compliance with ethical standards** All procedures performed in this study involving human participants were in accordance with the ethical standards of the responsible institutional committee on human experimentation and with the Helsinki Declaration of 1975, and the applicable revisions. Written informed consent was obtained from all study participants prior to inclusion in the study.

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