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Technical Note

A new method based on ICBM152 head surface for probe placement in multichannel fNIRS

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ABSTRACT

We propose a new probe placement method for multichannel functional Near Infrared Spectroscopy (fNIRS) based on the ICBM152 template, the most commonly used reference brain for neuroimaging. Our method is based on the use of a physical model of the ICBM152 head surface as reference scalp and its validity is supported by previous investigations of cranio-cerebral correlation. The method, intended for fNIRS group studies, dispenses with the use of individual MRI scan and digitizing procedure for each participant. The present approach offers a fast, simple, reproducible and straightforward method to place the probes on the head surface according to the MNI coordinates of the regions of interest with an average measurement error similar to those of previous methods. This ensures that fNIRS results can be readily compared within the neuroimaging community, both across studies and techniques.

Introduction

Functional near infrared spectroscopy (fNIRS) is a non-invasive neuroimaging technique used since the early 1990s (e.g., Villringer et al., 1993) to investigate hemodynamic brain activity. The fNIRS measures oxygenated hemoglobin (HbO) and deoxygenated hemoglobin (HbR) changes occurring in the cerebral cortex. It provides both reasonable temporal and spatial resolution, it is relatively insensitive to motion artifacts and it allows for an ecological experimental setting. However, the most relevant limitation of fNIRS resides in its inability to provide structural information about the brain. This drawback has become more relevant in recent years, because the earliest fNIRS instruments with only few channels (source–detector pairs) (e.g., Chance et al., 1993; Kato et al., 1993) have been replaced by those with a greater number of sources and detectors (multichannel fNIRS) that allow for a simultaneous functional investigation of a large part of the brain (e.g., Koizumi et al., 2003; Franceschini et al., 2006; Schecklmann et al., 2007; for a review, see Gibson et al., 2005). The latter approach clearly requires more stringent methods for cranio-cerebral correlation, in order to perform a reliable comparison of optical imaging data with the results of other neuroimaging techniques.

Since the proposal by the ICBM (International Consortium for Brain Mapping) of a functional probabilistic atlas (Mazziotta et al., 2000), there has been a constantly increasing use of a standard coordinate space for presenting the data obtained with tomographic functional brain mapping methods, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET). Usually, a normalization procedure is performed (by linear and/or nonlinear transformation) to fit individual functional imaging data into a common stereotaxic space referring to a template brain; two brain atlases are commonly used to normalize individual data to a common standard coordinate space: the Talairach (TAL, Talairach and Tournoux, 1988) and the Montreal Neurological Institute (MNI, Collins et al., 1994). While the Talairach atlas is based on a single brain, the MNI defined a new standard brain by averaging several magnetic resonance (MR) scans of human subjects (Collins et al., 1994; for a review, see Brett et al., 2002). The vast majority of functional neuroimaging data is currently presented in MNI space because it is a voxel-based, probabilistic template of the human brain (Mazziotta et al., 2001).

The current standard MNI template, known as the ICBM152 (Mazziotta et al., 2001), was obtained by averaging the high resolution scans of 152 normal subjects. Each MR scan (256×256 with 1 mm slices) was normalized to the MNI space using a 9 parameter affine transform. The final resolution of the ICBM152 template is $181\times217\times181$ with 1 mm isotropic voxels. According to Okamoto et al. (2004), fNIRS data should be presented in standard MNI coordinates to facilitate inter-study and cross-modal comparisons of functional neuroimaging data.

Therefore, it appears fundamental to obtain (directly or indirectly) information on the structural anatomy of the brain which is functionally investigated with fNIRS and to compare reliably the fNIRS results with those coming from other techniques. The direct solution consists in examining the cranio-cerebral structural

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correspondence by using the MR scan of each subject (or a subset of the subject sample). Although this method provides the highest precision possible, it is time consuming and most importantly, it makes the fNIRS dependent on MRI, decreasing its intrinsic value. MRI scanning is expensive and a scanner might not be available on the same premises of the fNIRS laboratory. As noted by Singh et al. (2005), opting out an fNIRS investigation because of the unavailability of individual MR scans would cause a conspicuous loss of valuable neuroimaging data.

The indirect method to establish cranio-cerebral correlation consists in using the international 10-20 system (Jasper, 1958) or its extended version, the 10-10 system (Chatrian et al., 1985). This is considered the de facto standard in electroencephalography (EEG), because it is a cheap and reproducible method for electrode placement. Essentially, this system describes the scalp of the subject through a series of locations obtained by measuring the distances between cranial landmarks. The main assumption behind the adoption of the 10-20 and 10-10 systems is that there is a systematic correspondence between head surface locations and the underlying cortical regions. Although prior studies investigated cranio-cerebral correlation (Blume et al., 1974; Morris et al., 1986; Homan et al., 1987), the study of Okamoto et al. (2004) was the first to provide a quantitative measure of such correspondence. The authors collected the MR scan of 17 subjects after having marked their 10-20 locations on the scalp, in order to identify them during MRI inspection. They then projected the 10-20 reference points at the cortical level, obtaining a probabilistic distribution of the 10-20 locations in MNI coordinates. Interestingly, they found that 10-20 reference points can be used to estimate the correspondent MNI coordinates (both for the head surface and the cortical projections) with an error that was less than 1 cm (except for the occipital regions, O1 and O2, that exhibited the greatest individual variation, tending to be less reliable).

The seminal study of Okamoto et al. (2004) prompted several investigators to use and refine the cranio-cerebral correlation method (Okamoto and Dan, 2005; Singh et al., 2005; Jurcak et al., 2007; Tsuzuki et al., 2007; Koessler et al., 2009; Custo et al., 2010). Most notably, Tsuzuki et al. (2007) proposed a virtual registration method of fNIRS data onto MNI space that involved neither scanning the subjects with MRI nor digitizing their head surface. They used flexible holders and tested them on human heads and in a virtual environment. Placement of a probe holder on the scalp with the method of Tsuzuki et al. (2007) requires running a simulation of the holder's deformation and registering the position of probes and channels. That is, a virtual holder deformation algorithm is used to mimic the deformation of the holder on the scalp. A set of synthetic heads and brains is generated by randomly combining head sizes and shapes from the un-normalized scans of the NFRI_R17 (National Food Research Institute Reference database, 17 MR individual scans; for details, see Okamoto et al., 2004). For each synthetic head and brain, the virtual holder deformation algorithm is used to estimate the position of fNIRS head surface points of the probes and the cerebral projections of the channels. The data on the position of probes and channels obtained from the synthetic head and brain are transformed to the original MR dataset, and then to MNI space (for details, see Okamoto and Dan, 2005). This procedure is repeated 1000 times, in order to simulate head size and shape variability across population; afterwards, statistical analysis of the MNI coordinates is performed to estimate the most likely location of each channel and its variability. Estimated locations are then anatomically labeled by using conventional brain atlases. Remarkably, they showed that the spatial error implied by different head sizes and shapes of the subjects can be minimized by the use of flexible/elastic probes. Indeed, they showed that the precision of their method was comparable to that of a previous probabilistic registration method performed with a 3D-digitizer (Singh et al., 2005). However, as the authors themselves noted, the use of a simulated dataset to assess the inter-subject variability and the procedure described in their study is not completely straightforward, since it requires the experimenter to provide different parameters and to perform several adjustments for each virtual holder registration.

Our aim was to create a method that combined the operative advantages of Tsuzuki et al.'s (2007) own method with a greatly improved usability. The core of our proposal stems from the fact that the ICBM152 template is the most common stereotaxic platform for tomographic functional brain mapping methods (Mazziotta et al., 2001; for a review, see Brett et al., 2002), since it is the current standard MNI template. If the neuroimaging community has adopted the "brain" represented in the ICBM152 template as the common reference brain, its head surface should be the best candidate to become the common reference head surface. From this point of view, the introduction of a physical model of the ICBM152 head surface could provide several benefits in the probe placement process. For instance, it could help to avoid using a virtual holder deformation algorithm, because the deformation of the holder would be accounted by its placement on the physical model itself; furthermore, it could provide a direct link between the virtual space of MNI stereotaxic coordinates (and the ICBM152 template) and the physical space of fNIRS channel positions. Classical probe location estimation methods (e.g., Tsuzuki et al., 2007) provide an estimate of the MNI coordinates corresponding to the channels only after the probe has been placed. In contrast, with the adoption of a physical model of ICBM152 head surface, experimenters could use the MNI coordinates of the regions of interest to directly guide the probe placement process on the physical model.

Therefore, we propose a novel probe placement method explicitly designed for functional group analysis in multichannel fNIRS, based on a physical model of the ICBM152 template. The presented method pursues three main purposes. First, it must be a fast, simple, reproducible and straightforward method to execute a reasonably precise probe placement. Second, it must be able to avoid the digitizing procedure for every subject and to eliminate the need of the MR of individual subjects, thus making fNIRS group analysis MRI-free. Finally, it needs to ensure an optimal compatibility of the fNIRS results with other neuroimaging results that adopt the MNI coordinates to locate the cerebral regions. Accordingly, our method allows to register fNIRS optode and channel positions directly to the ICBM152 template, and therefore to the MNI stereotaxic coordinate system.

The paper is organized as follows. First, we describe how to create a physical model of the head corresponding to the ICBM152 brain template. We then describe how the physical model is used to find the best placement of the fNIRS probes in relation to the cerebral regions to be investigated. Finally, we provide a practical example of setting up an fNIRS bilateral recording from the parietal cortex, which is also used as an additional validation of the procedure.

Method

Physical model of the ICBM152 head

In order to create a physical model of the head corresponding to the ICBM152 brain template, we executed a series of operations, mostly performed with 3D-DOCTOR ver. 3.5 (ABLE SOFTWARE CORP., http://www.3d-doctor.com), an advanced 3D modeling, image processing and measurement software. The MNC file of ICBM152 template, which is freely available (http://packages.bic.mni.mcgill.ca/tgz/mni-models_icbm152-lin-1.0.tar.gz) at 1 mm^3 resolution, has been converted in ANALYZE format using LONI Debabeler, ver. 2.8 (http://www.loni.ucla.edu/Software/Debabeler) and then in a sequence of slices (tiff format) with SPACE, ver. 94h.2 (http://lcni.uoregon.edu/~mark/Space_program.html), in order to ensure the maximum compatibility with 3D-DOCTOR. The tiff file of ICBM152 containing the slices was loaded into 3D-DOCTOR, then a sequence of

operations has been performed: we defined the object of interest as the external border for each slice using an edge detection algorithm (Fig. 1); the borders were then automatically selected using the interactive segmentation tool, generating preliminary object boundaries which were subsequently optimized by adjusting the selection threshold. The same selection criteria have been applied to all slices, giving as result a homogeneous selection of the boundaries (red lines in Fig. 1).

After this intermediate selection stage of the boundaries, the definitive selection was achieved by automatically simplifying the boundaries (using a built-in function of 3-D DOCTOR), in order to eliminate the presence of crispy edges. Once the selection stage was completed, we created a 3D virtual model of ICBM152, the ICBM152-VM (virtual model), using the fast complex surface rendering. The development of a virtual 3D model is necessary because standard MR files (e.g., hdr-img, MNC), being a sequence of 2D images, are not an appropriate input for 3D printing. Thus, the ICBM152-VM is a virtual 3D polygonal mesh model of the ICBM152 template's head surface, reproduced in 1:1 scale. The ICBM152-VM has been stored in STL (Stereo Lithography) format and is available at http://ccnl.psy.unipd.it/ICBM152head.html. The result is shown in Fig. 2 (1st row). The physical model was realized by a company specialized in 3D printing. Starting from our STL file, the company produced at a very affordable cost (below 300 Euro) a 1:1 model of ICBM152-VM in epoxy resin, with a precision of 82 micron. The resulting model, the ICBM152-PM (Physical Model) is shown in Fig. 2 (2nd row), and in a short video in the Supplementary Material).

For comparative purposes, we located all 10-10 points using the Unambiguously Illustrated (UI) 10-10 system (for a detailed explanation of this system, see Jurcak et al., 2007) on the head surface of the ICBM152-PM. We digitized the 10-10 points on the scalp (Fig. 2, 3rd row) and their cerebral projections (at a depth of 20 mm; see following sections for further details) (Fig. 2, 4th row) with a frameless stereotaxic neuronavigation system (Brainsight-Frameless™, version 1.7, Rogue Research Inc., Montreal, Quebec, Canada) based on Polaris Vicra™ (Northern Digital Inc, Ontario, Canada) optical 3D digitizer.

We compared the MNI coordinates corresponding to the 10-20 points subset obtained with our procedure to those found in the study of Okamoto et al. (2004); the mean difference between the MNI coordinates was negligible (mean ± standard deviation, hereafter SD: 0.14 mm ± 5.5 mm for scalp positions, Table 1; 0.84 mm ± 10.55 mm for cerebral projections, Table 2). The MNI coordinates of 10-10 reference points are reported in the Supplementary Material.

In the following paragraphs we describe two procedures that need to be executed when the ICBM152-PM is available: *ICBM152-PM Setup* and *Holder Setup*. Note that *ICBM152-PM setup* must be performed only once, whereas *Holder Setup* must be performed once for each experiment. To summarize, what is needed for our method consists in the ICBM template, the ICBM152-PM (physical model of the ICBM152 head), one of the many commercially available neuronavigation systems with a 3D digitizer (see Supplementary Material for a list of other suitable systems), and a flexible/elastic holder.

ICBM152-PM Setup

Setting up the ICBM152-PM requires the following steps:

1) The ICBM152 template must be loaded onto the neuronavigation software and the four primary cranio-metrical landmarks need to be marked: Nasion (Nz), Inion (Iz), and the left-right periauricolar points (LPA-RPA). We chose as LPA-RPA the point determined between the upper edge of the tragus and the daith (for details on other possible PAs see Jurcak et al., 2007). Nz and Iz have been chosen by a careful visual inspection of the ICBM152 template. The MNI coordinates of these four cranial landmarks used in our 10-10 measurement are shown in Table 1.
2) The four primary cranio-metrical landmarks must be located on the ICBM152-PM head surface. At this point, the experimenter must check the validity of the four reference points by "navigating" over the head surface with the tracking pen. Note that there should be a close correspondence between the position of the tracking pen on the ICBM152-PM and that indicated by the digitizing software in the ICBM152 MR. If such correspondence is not met, this step must be repeated.
3) The 10-20 (or 10-10) reference points must be marked on the scalp of the ICBM152-PM and then digitized with the tracking pen (in our example, we marked the 10-10 reference points). The cerebral projections of the 10-10 positions are individuated by using the common "*tip-offset*" function of the neuronavigation software: when the tracking pen is placed on a given head surface point, this built-in function provides in real time the MNI coordinates of the cortical region underlying the head surface

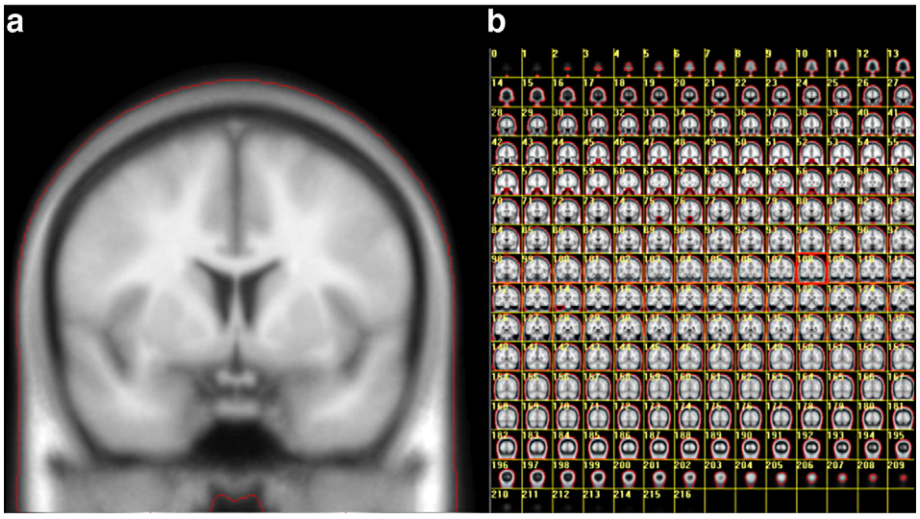

Fig. 1. Screenshot of the boundary selection process: (a) a magnified slice of the ICBM152 template. The red border corresponds to the boundary selected to create the ICBM152-VM. (b) Thumbnails of the slices with the corresponding boundaries (red lines).

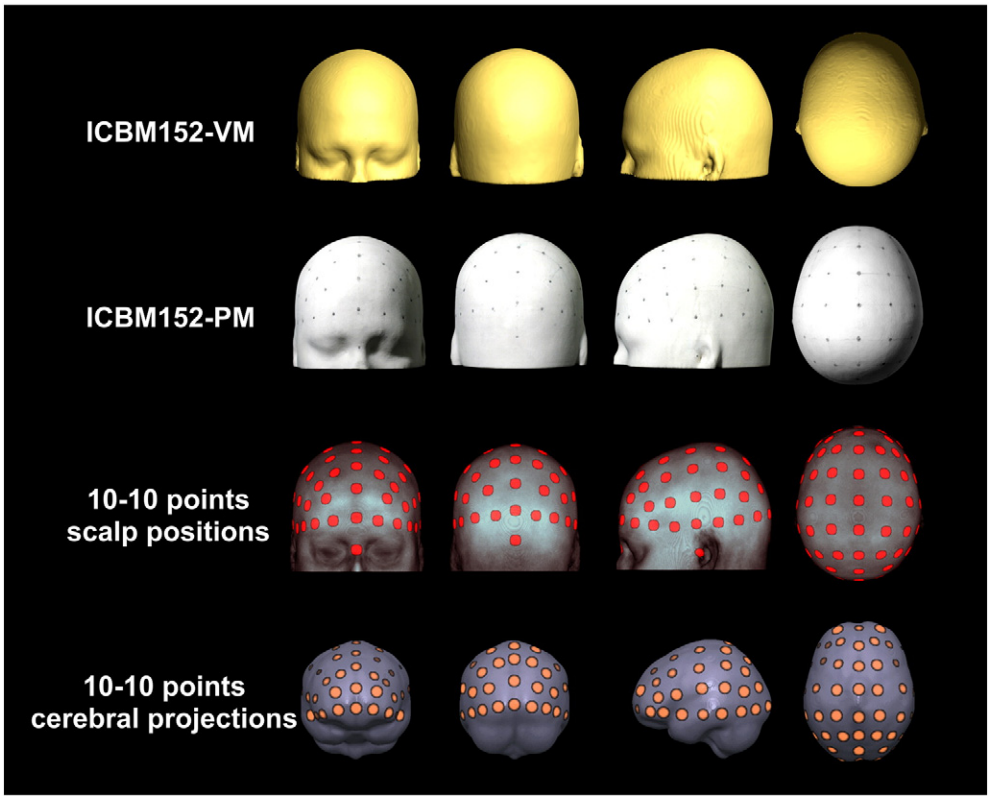

Fig. 2. Illustration of the models. First row: the ICBM152-VM. Second row: the ICBM152-PM. Third row: the 10-10 points scalp positions (red circles) superimposed on the ICBM152 template head surface. Fourth row: the 10-10 points cerebral projections (orange circles) superimposed on the ICBM152 template brain. The procedure to visualize the points is described in Cutini et al. (2008). The points have been created with a 1-cm Gaussian blurring, to reproduce the spatial resolution of fNIRS. All the models are in the same view order (from left to right): front, back, left and top.

point at a chosen depth, which is selected by the user. Note that when calculating the cerebral projection of the digitizing pen, the orientation of the pen influences the cerebral projection estimation; thus, the tracking pen should be always normal (that is, perpendicular) to the scalp in contact with the tracking pen. With appropriate care, examiner-dependent error due to the orientation of the pen can be considered negligible (Poggi et al., 2003; Reinges et al., 2000). Note also that cerebral projections obtained with the tracking pen are commonly used in TMS (Transcranial Magnetic Stimulation) studies.

When choosing the tip-offset value, researchers should consider two factors: (i) the penetration depth of near infrared light depends on the source–detector distance (Choi et al., 2004; Patterson et al., 1995); (ii) the average cortical surface depth varies across regions, as shown by Okamoto et al. (2004). Therefore, the source–detector distance should be chosen in relation to the depth of the cortical regions that the experimenters plan to investigate, in order to maximize the number of photons passing trough the regions of interest. From a general point of view, using the location information of cortical surface of the ICBM152 MR template can be considered a reasonable solution. In the practical example presented below, the source–detector distance in the holders was set to 35 mm in order to investigate the parietal cortex, which has an average cortical surface depth of 17 mm (Okamoto et al., 2004). Considering that the average cortical thickness is around 3 mm (Hutton et al., 2008), we chose a tip-offset value of 20 mm.

Note that the MNI coordinates of the 10-10 points and the cerebral projections reported in the present article are not meant to be a reference, because they have been used only for comparative purposes. Indeed, although we encourage adopting the UI 10-10 system (Jurcak et al., 2007), the experimenters who are willing to use our method are free to use any procedure to locate scalp positions, on condition that the measurement procedure used for ICBM152-PM will be the same of that used for the subjects; similarly, the tip-offset value should be varied according to the regions under investigation.

Holder Setup

The aim of the Holder Setup procedure is to find the best placement of the fNIRS probes in relation to the cerebral regions to be investigated. Starting with the MNI coordinates of the region(s) of interest, the procedure finds the set of 10-20 (or 10-10) reference points that must be used as spatial constraints to place each holder on the scalp of human subjects and the exact MNI coordinates of each channel. When placing multiple holders (e.g., one holder on the frontal lobe and another one on the parietal lobe), this operation should be repeated for each holder to obtain its specific set of 10-20 (or 10-10) points.

As shown by Tsuzuki et al. (2007), the mere adoption of elastic or flexible probes minimizes the error caused by the different sizes and shapes of the subjects' heads. However, this holds for a holder surface that does not exceed that of the 3×5 holder (i.e., 135 cm^2) employed by Tsuzuki et al. (2007). We therefore recommend using multiple small holders when recording from a large number of sources and detectors (in the example reported below we used two symmetrical holders of about 90 cm^2 each).

The Holder Setup procedure, which must be performed only once per experiment, requires the following steps (for each holder):

Table 1
Comparison between the MNI coordinates of 10-20 scalp positions found by Okamoto et al. (2004) and those found in our registration. The nomenclature of the points is the same of Jurcak et al. (2007). The MNI coordinates of the four primary reference points are showed at the bottom of the table. Mean difference and standard deviation are reported in mm.

MNI coordinates of 10-20 scalp positions						
	Position Okamoto et al. (2004)			Position ICBM152-PM		
Site	*x*	*y*	*z*	*x*	*y*	*z*
Fp1	−26	84	0	−28	83	−5
Fp2	32	81	0	31	84	−5
Fz	0	53	71	0	58	66
F3	−43	58	40	−50	55	39
F4	47	57	40	50	55	41
F7	−69	38	−6	−68	41	−12
F8	71	36	−8	69	41	−12
Cz	1	−13	101	0	−9	100
C3	−63	−13	70	−66	−11	63
C4	64	−15	70	69	−11	63
T7	−85	−21	−11	−80	−16	−10
T8	86	−26	−9	81	−17	−10
Pz	0	−77	89	0	−82	78
P3	−47	−88	59	−52	−80	54
P4	45	−88	60	53	−80	54
P7	−72	−72	1	−71	−72	−5
P8	71	−75	4	70	−72	−5
O1	−32	−113	17	−26	−111	3
O2	28	−113	19	27	−109	3
	Mean difference			−0.14 mm		
	Standard deviation			5.5 mm		

Primary reference points	*x*	*y*	*z*
Nz	0	84	−43
Iz	0	−114	−30
LPA	−75.09	−19.49	−47.98
RPA	76	−19.45	−47.7

Table 2
Comparison between the MNI coordinates of 10-20 cerebral projections found by Okamoto et al. (2004) and those found in our registration. Mean difference and standard deviation are reported in mm.

MNI coordinates of 10-20 cortical projection points						
	Position Okamoto et al. (2004)			Position ICBM152-PM		
Site	*x*	*y*	*z*	*x*	*y*	*z*
Fp1	−22	70	0	−22	65	−2
Fp2	28	69	0	23	66	−3
Fz	1	41	54	0	44	51
F3	−36	49	32	−36	43	30
F4	40	48	32	36	44	32
F7	−55	34	−4	−47	36	−7
F8	57	31	−4	47	39	−8
Cz	1	−15	74	0	−11	80
C3	−52	−16	58	−52	−11	49
C4	54	−18	58	54	−11	49
T7	−70	−21	−11	−61	−16	−10
T8	72	−25	−8	63	−17	−10
Pz	0	−62	65	0	−71	64
P3	−40	−76	47	−41	−69	45
P4	37	−75	49	41	−69	44
P7	−62	−65	1	−53	−65	−6
P8	59	−68	4	53	−65	−5
O1	−27	−100	13	−21	−98	1
O2	24	−101	14	23	−97	1
	Mean difference			−0.84 mm		
	Standard deviation			10.55 mm		

1) The MNI coordinates corresponding to the cerebral region(s) of interest (reference coordinates, hereafter $Coord_{REF}$) need to be chosen by examining functional data (fMRI and/or PET) coming from experiments which address on the same research issue. These coordinates will guide the probe placement.
2) After the setup of the ICBM152 template onto the neuronavigation software (by digitizing the four primary cranio-metrical landmarks, as in step 2 of *ICBM152-PM Setup*), the head surface projection of each $Coord_{REF}$ must be marked on the ICBM152-PM (using the tip-offset function, the point is individuated by skimming the tracking pen through the head surface).
3) When the head surface projections of $Coord_{REF}$ points have been found, the holder is tentatively placed over them (note that channels always refer to the cerebral projection of the midpoint between each source–detector pair, while sources and detectors always refer to head surface). Then, the position of each channel is digitized (with the tracking pen and the tip-offset function enabled) in the midpoint of the corresponding source–detector pair (see Fig. 3a and b) to obtain its MNI coordinates. This operation allows to individuate the coordinates of the channel (hereafter $Coord_{CH}$) that is closest to a given region of interest. Probe placement can be improved by slightly changing the position and/or the orientation of the holder to minimize the difference between $Coord_{REF}$ and $Coord_{CH}$. A new set of $Coord_{CH}$ must be obtained every time the probe orientation/position is changed and the procedure must be repeated until the mean difference between $Coord_{REF}$ and $Coord_{CH}$ is below 5 mm (the lowest SD of the cerebral projections measurement values found by Okamoto et al., 2004). At that point, the remaining channels have to be digitized to obtain the final set of MNI coordinates of the channels. The position of the sources and detectors on the ICBM152-PM head surface must be digitized too.
4) The head surface points corresponding to sources and detectors (digitized on the ICBM152-PM in the previous step) are used to find the 10-20 (or 10-10) reference points that will guide probe placement on human participants during the experiment. Thus, the experimenter needs to search for three 10-20 (or 10-10) reference points close to any source or detector on the ICBM152-PM, so that the holders can be placed over the scalp in a reproducible way across subjects (e.g., source A must be placed on C3 and source B must be placed on F3). An example of such procedure with two symmetrical holders is provided below (also see Cutini et al., 2008). Visual inspection can readily provide the points that are best suited as spatial constraints; nonetheless, in the Supplementary Material we provide a Matlab function (Matlab R2009b, The Mathworks Inc., Natick, Massachusetts, USA) that, given the MNI coordinates of 10-10 scalp points and the MNI coordinates of sources and detectors, returns the n sources or detectors closest to any 10-10 points. Note that the use of three reference points represents the best compromise between time-saving and accuracy. Poggi et al. (2003) investigated the measurement error implied by neuronavigation and found that the mean localization error decreased about 1 mm when the number of reference points increased from 3 to 9. Thus, using more than three points would produce a negligible increase in accuracy.[1]
5) Finally, all the other channels need to be anatomically labeled; for each channel, the corresponding cerebral region needs to be identified. While the regions covered by the channels corresponding to the set of $Coord_{CH}$ are already known, the cerebral regions corresponding to the other channels can be easily identified by using a 3D anatomical atlas (e.g., Tzourio-Mazoyer et al., 2002), or by searching for regions with similar coordinates in the Brede Database (http://neuro.imm.dtu.dk/services/jerne/brede).

[1] More generally, given a single-point measurement error e, accuracy based on n reference points is proportional to $e/\sqrt{k}$, where k is the number of triangulations that can be made with the n points: $k = \frac{n(n-1)}{2}$.

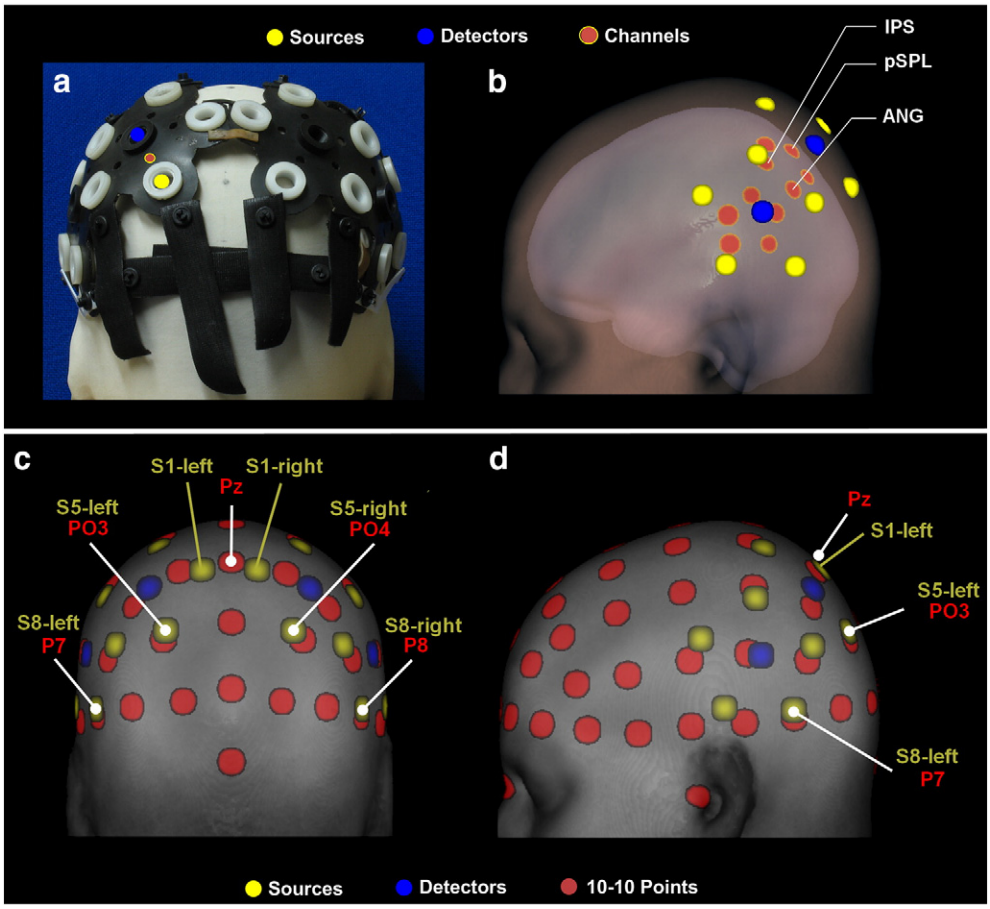

Fig. 3. Illustration of the probe placement in the Holder Setup for fNIRS bilateral recording from parietal cortex: (a) a photo of the holder placed onto the ICBM152-PM (occipital view). The circles on a source (yellow), a detector (blue) and on the hole corresponding to a channel (red with yellow border) have been added for illustrative purposes. (b) An illustration of the probe location on the ICBM152 template brain with the head in transparency. The yellow and blue circles correspond to the position of sources and detectors on the head surface, respectively. The red circles with yellow border correspond to the position of the channels on the cerebral cortex. The channels that cover the regions of interest are indicated with the white lines (IPS, intraparietal sulcus; pSPL, posterior superior parietal lobule; ANG, angular gyrus). (c and d) Illustration of the probes and their relationship with 10-20/10-10 points on the ICBM152 template (c, occipital view; d, left temporal view). The two figures show the sources (yellow circles), the detectors (blue circles) and the 10-10 points (red circles). The sources (left/right S1, S5 and S8) and the 10-20/10-10 points (Pz, P7/8 and PO3/4) that are used to create the triple spatial bind to ensure a reproducible probe placement across subjects are indicated in the figure.

At this point the entire procedure is completed. When testing human participants, the holders must be placed using the 10-20 (or 10-10) system, according to the resulting spatial bind obtained in step 4. Unlike the method of Singh et al. (2005), which required a Real World–MNI coordinates transformation, our method does not involve any affine transformation. The ICBM152-PM is characterized by a 1:1 ratio between Real World and MNI coordinates; thus, after the registration of fiducial points of the ICBM152-PM (with the ICBM152 MR loaded onto the neuronavigation software; see step 2 of *ICBM152-PM Setup*), the neuronavigator itself provides in real-time the MNI coordinates of the scalp point in contact with the tracking pen.

It is worth reiterating that the holder setup must be performed only once per experiment and no MRI scan or digitizing procedure is needed for human participants to use this method (specifically intended to fNIRS group analysis).

A practical example: Holder Setup for fNIRS bilateral recording from parietal cortex

We provide here a practical example of how our method can be used to find the best probe placement for investigating a specific set of brain regions. This example is also used as an additional validation of our method.

The regions of interest are parietal areas that are known to be involved in numerical cognition. An influential meta-analysis of the neuroimaging studies (Dehaene et al., 2003) has revealed three main parietal regions related to numerical processing: the left angular gyrus (ANG), the bilateral intraparietal sulcus (IPS) and the bilateral posterior superior parietal lobule (pSPL). Therefore, the MNI coordinates indicated in the meta-analysis were used as $Coord_{REF}$ for the probe placement procedure (the TAL coordinates reported in the meta-analysis have been converted in MNI coordinates with the transformation algorithm "tal2icbm_spm.m"; for details see Lancaster et al., 2007). We planned to cover all these regions by symmetrically placing two identical holders with a source–detector distance of 35 mm, one for each hemisphere. The probe placement on the ICBM152-PM is shown in Fig. 3a.

By using the tip-offset function of the neuronavigation software that allows to estimate the cerebral projection of a given head surface point, we identified the head surface points above the regions of interest, and we placed the holders on the ICBM152-PM to broadly cover them. Then, we acquired the MNI coordinates of the channels by inserting the tracking pen into the hole corresponding to the midpoint of each source–detector pair, in order to check the MNI coordinates of their cerebral projections (using a tip-offset value of 20 mm) (see Fig. 3a and b), and we individuated the channels that were closest to the regions of interest (see Fig. 3b). Probe placement was optimized by

iteratively searching for a location/orientation that minimized the difference between the MNI coordinates of the channels ($Coord_{CH}$) and those corresponding to the regions of interest ($Coord_{REF}$). We found a satisfactory position and orientation of the holders (see Fig. 3a) in about 15 min, which resulted in a minimal difference between $Coord_{REF}$ and $Coord_{CH}$ (1.96 ± 3.95 mm).

Next, we digitized the position of all the sources (S1 to S8) and detectors (D1 to D4) on the ICBM152-PM head surface, as well as the position of the other channels to obtain the final set of MNI coordinates of the channels (including the $Coord_{CH}$ channels; all the channels are shown in Fig. 3b). At this point, we searched for 10-10 reference points close to any source or detector on the ICBM152-PM head surface. In this case, we established three spatial binds for each holder: Pz had to be in the middle between S1-left and S1-right, S5-left/right had to be as close as possible to PO3/PO4, and S9-left/right had to be as close as possible to P7/P8, respectively (see Fig. 3c and d). Note that these two sets of spatial constraints will be used to place the holders over the scalp in a reproducible way across human subjects. As noted before, using more than three points as a spatial constraint would produce a negligible increase in accuracy (Poggi et al., 2003); thus, a set of three points (for each holder) represents the best compromise between time saving and accuracy.

Finally, we identified the cerebral structures covered by the channels by using the Brede database (except for the channels that were specifically placed on IPS, ANG and pSPL).

To provide an additional validation of our method, we measured the spatial error implied by the probe placement procedure on three adult human subjects (two females). For each participant, the MR scan (T1-weighted MR scan was obtained from each participant using a GE Signa 3T System, $1.3 \times 1.3 \times 1.3$ mm, sagittal acquisition) was normalized to ICBM152 template through a 12-parameter affine transformation (performed with SPM8, http://www.fil.ion.ucl.ac.uk/spm/software/spm8) and loaded onto the neuronavigation software. We placed the holders on each subject according to the sets of selected 10-10 points (Pz, P7/8 and PO3/4) and we then acquired the MNI coordinates of the channels by using the neuronavigation system. The mean distance from the MNI coordinates of the channels registered on human subjects and the set of MNI coordinates found on the ICBM152-PM (depicted in Fig. 3b) was less than 1 cm (3.75 ± 7.49 mm). This deviation is well below the spatial resolution of fNIRS and it is perfectly in line with the findings of Okamoto et al. (2004), despite the variability in head size and shape of the subjects (the SD of head circumference was 20.82 mm).

Discussion

The present method has three main features: (i) it is a fast, simple and straightforward method to obtain a precise probe placement for fNIRS recording; (ii) it does not require individual MRI scans, making fNIRS group analysis independent from individual MR scans, and it does not require the digitizing procedure for every subject; (iii) probes and channels are located in MNI coordinates in a straightforward way, ensuring that fNIRS results can be readily compared with other neuroimaging data.

The proposed method is straightforward and easily reproducible: the digitizing procedure on the ICBM152-PM must be performed only once, and the holder setup must be performed only one time per experiment. Our approach finds its theoretical foundation in a number of previous studies. First, the results of Okamoto et al. (2004) can be used as a benchmark for the strength of the correlation between the head surface and the underlying cerebral structures. The negligible difference between the MNI coordinates of 10-20 points found in their work and those found with our method shows that their conclusions regarding the precision of cranio-cerebral correlation can be readily generalized to our approach. Second, the combination of our method with the use of deformable holders that minimize the error due to different size and shape of head surfaces (Tsuzuki et al., 2007) can yield an average error comparable to that observed in previous investigations (Okamoto et al., 2004; Singh et al., 2005; Tsuzuki et al., 2007). This implies that the average measurement error introduced by our method remains below the spatial resolution of multichannel fNIRS and is comparable to that of the other methods (although any indirect method should be used with caution when investigating the occipital lobe, as mentioned in Introduction). As a result, the method proposed here translates into valuable time and money savings, with no sensible loss in precision for fNIRS experiments that focus on group analysis. Conversely, it should not be used for single subject analysis, where very precise anatomical information is mandatory.

We believe that the ICBM152 is the best template for a description of scalp positions and their correlation to MNI coordinates of the underlying cerebral structures. As noted before, the ICBM152 template has been adopted as the reference brain by the neuroimaging community (Mazziotta et al., 2001; for a review, see Brett et al., 2002). It seems therefore reasonable to use the scalp derived from this template as a reference head surface for fNIRS probe placement. Nevertheless, we note that other templates could be used with our method, such as the more recent ICBM452 that represents the average of a larger group of subjects than the ICBM152. A transition to this new template would be warranted only when it becomes the new standard. Another possible choice would have been the COLIN27 template (Holmes et al., 1998), which was created by registering and averaging 27 high resolution scans of the same individual in stereotaxic space. This choice may be optimal for diffuse optical tomography (DOT) where sources and detectors are usually placed in an overlapping manner and spatial resolution might be increased. As noted by Custo et al. (2010), the use of the COLIN27 template enables to precisely label connective tissue, fat, skin, and white matter. However, it would suffer from the "single brain" criticism that applies to the Talairach brain (Talairach and Tournoux, 1988), thus making it less appropriate as a template for probabilistic cranio-cerebral correlation. Our method is explicitly designed for "classical" multichannel fNIRS, usually subjected to channel-wise analysis. The rationale for the attempt to provide a straightforward conversion of fNIRS data to MNI space is that the same channel (source–detector pair) will fall, on average, on the same MNI coordinates of all subjects tested. It is worth noting that this assumption is identical to that concerning voxel-wise analysis of fMRI data. From this point of view, probe placement with our method follows the same logic, because the position of each fNIRS channel is registered on the ICBM152-PM, and therefore directly on the MNI stereotaxic space. The stereotaxic MNI brain coordinates system serves as a common spatial platform for data alignment of tomographic neuroimaging techniques; therefore, the use of MNI coordinates rather than 10-20 (or 10-10) reference points to locate the brain regions investigated with fNIRS ensures optimal data sharing within the neuroimaging community both across studies and techniques.

One possible caveat is that producing a physical model from a virtual one could be seen as a sort of back step, because historical development proceeded from a physical model, the Talairach brain, to a virtual one, the ICBM152. However, we believe that our work represents the last step forward to fill the gap between the virtual space of ICBM152 and the physical space in which 10-20 reference points are used. As clearly shown in our practical example of holder setup, the physical model of ICBM152 can be a very useful tool for fNIRS users. Our method provides maximum adherence of fNIRS data to the standard used by neuroimaging community and it therefore represents a valuable methodological improvement of the fNIRS technique.

It is not crucial to adopt a specific method to precisely define 10-20 locations and indeed any procedure can be used to mark scalp positions, on condition that the measurement procedure used for ICBM152-PM will be the same of that used for the subjects. Since the

10-20 system is very sensitive both to initial reference points and different methods used (see Jurcak et al., 2007), the resulting coordinates can vary according to the method used to locate the reference points. As mentioned earlier, the depth-penetration of the tip-offset function should be chosen by considering both the source–detector distance, which influences the near infrared light penetration depth into the scalp (Patterson et al., 1995; Choi et al., 2004) and the average cortical surface depth of the areas covered by the probes, which varies across regions (Okamoto et al., 2004). As a consequence, the MNI coordinates of the 10-10 points and the cerebral projections reported in the present article should not be used as a reference.

While our method should be viewed as an alternative to that of Tsuzuki et al. (2007), it is rather complementary to Custo et al.'s (2010) method for DOT analysis, which is commonly based on a large number of very high densely-placed sources and detectors (e.g., Zeff et al., 2007).

Our method needs the digitizing procedure only for the ICBM152-PM, while the method of Custo et al. (2010) requires the digitizing procedure of all 10-20 points and probes for each subject (which are then normalized to MNI space using a 3×4 affine transformation). While the individual digitizing procedure is a necessary component of their method, it is not critical for spatial resolution in multichannel fNIRS voxel-wise analysis. As shown by previous studies, the estimation accuracy provided by the virtual registration method of Tsuzuki et al. (2007) is comparable to the results obtained with a probabilistic registration method using a 3D-digitizer (Singh et al., 2005). The requirement of individual digitizing procedure is likely to become an issue over the next few years, because most fNIRS instruments will exceed 50 channels: as the number of channels increases, the individual digitizing procedure is more time consuming. In this regard, it is worth reiterating that our method requires the use of holders with a surface not exceeding that of the holder employed by Tsuzuki et al. (2007) to warrant a comparable accuracy level. However, this limitation can be readily circumvented by using multiple smaller holders.

For what concerns the virtual registration method of Tsuzuki et al. (2007) (see Introduction for a detailed description of the method), its main breakthrough was to reveal the potential of using deformable/flexible holders. Its main drawback resides in its complexity: as the authors themselves note, its practical use remains a major obstacle. For example, the procedure implied by their method requires the user to provide many parameters and small adjustments for each virtual holder registration. It is worth noting that our method does not imply any virtual deformation algorithm, because with the present method the position of the probes is measured by placing the holder on the ICBM152-PM. Although the iterative search of the best probe placement (to maximize CoordCH and CoordREF correspondence) could be performed automatically if a virtual model was used instead of a physical one (probably resulting in saving-time), we strongly believe that the effort needed to search the best probe location on the ICBM152-PM without an algorithm or a virtual model is well rewarded by the avoidance of the technical difficulties caused by the adoption of a virtual deformation algorithm of the holder, as noted by Tsuzuki et al. (2007).

Moreover, setting aside the issue of usability, there is a key conceptual difference between our method and that of Tsuzuki et al. (2007). Their virtual registration method provides an estimate of the most likely MNI coordinates corresponding to the channels after the holder has been placed. This logic is completely reversed in our method. That is, the MNI coordinates of the regions of interest are driving the probe placement process, and 10-20 reference points are only used to ensure a reproducible placement across subjects.

It is worth noting that our method is best suited for fNIRS studies based on regions of interest, where probe placement is guided by the location of specific anatomical sites (derived from a brain atlas) or activation foci of other brain imaging studies. Although this could be seen as a limitation of our approach, it is important to recognize that dense multi-channel whole-brain recording is not the current standard in fNIRS research. Therefore, a ROI-based approach to probe placement is an optimal compromise for any fNIRS setup that does not allow for whole-brain recording. However, nothing prevents the user from placing some or all probes using only the 10-20/10-10 points as a guide and then calculate the MNI coordinates of the channels using our method. This would be similar to other post-hoc normalization procedures, while preserving the high usability of our method. Note that a common procedure in fNIRS studies was to simply place the holder on the scalp by using a single 10-20 reference points (e.g., the middle of the holder is placed on Cz) and neuroanatomical localization of the channels could only very broadly inferred.

In conclusion, it is worth noting that any indirect method, whether based on a virtual model and complex algorithms (e.g., Tsuzuki et al., 2007) or on a physical model like ours, is characterized by its own strengths and weaknesses. While some researchers will prefer the former approach, it is conceivable that others will like the hands-on approach proposed here. Indeed, we believe that our method represents the optimal compromise between precision and usability for fNIRS investigations. The only additional instruments that it requires are the physical model of the ICBM152 head and one of the commercially available 3D-neuronavigation systems. We consider our method as the most simple and straightforward approach to perform probe placement for fNIRS group studies, with a spatial error that is comparable to that of other methods that are more sophisticated but difficult to implement.

Supplementary materials related to this article can be found online at doi:10.1016/j.neuroimage.2010.09.030.

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