mark (or 'signature') that may be used to locate primary visual cortex. This technique may then be used, with soon to be available, higher resolution PETT scanners (e.g. PETT-VI), for more detailed studies of primary visual cortex topography and stimulus preferences, as well as an aid in beginning to study extra-striate visual areas in humans.

The present experiment was designed to study the topographic structure of human primary visual cortex, within the constraints outlined above. A quantitative model of human striate cortex topography, based on data from lower primates and human psychophysical data[3,11,12] was used to guide the construction of the visual stimulus. This stimulus consisted of a spiral pattern of 'line segments' or 'edges'. The size of the line elements making up the stimulus was increased linearly with eccentricity, in order to match the value of cortical magnification factor at all eccentricities. Estimates of human cortical magnification factor3 suggest that the cortical representation of a circle at about 10° of eccentricity divides the striate cortical representation into a central and peripheral region of roughly equal areas. This circle, at 10° of eccentricity, and the horizontal meridian, divide the striate cortex representation (one hemisphere) into 4 equal areas. The computer animation used in this experiment utilized a configuration of this sort (Fig. 1) to stimulate an on–off pattern in striate cortex which consisted of a coarse *2 x 2* 'checkerboard', in one hemisphere. This constituted the 'signature' which was to be located in the PETT data. A computer animation was constructed by generating a stimulus configuration as described above (and shown in Fig. 1) onto a television monitor, and then filming (with a computer controlled camera) frame by frame onto 8 mm film.

Eye position of subjects was monitored and controlled by requiring subjects to report verbally the identity of small test letters (1° in size) which were randomly presented at the fixation point. These test letters were constructed by the same computer graphic method as the line elements of the stimulus, and were part of the same computer animation. The interval between presentation of the test letters was random, with an average of 1 s. The duration of presentation was 200 ms. Since this is too short a time for a saccadic eye movement, and since the letters were too small to be correctly identified from non-foveal fixations, a high score (>80%) on this task implied an accurate and reliable eye fixation. In addition, this

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Fig. 1. Top: on the top left is shown a single frame from the computer animation which was used as a stimulus. Not shown is a small fixation letter, which was presented at the center of the semi-circular pattern. In this example, the superior central and inferior peripheral right hemi-fields were stimulated. The size of the pixels used in the display increased linearly from the fovea, in order to match receptive field size and spatial frequency sensitivity of cortical cells at all eccentricities. The size of the pixels in the central field representation was about 1/5 degree (i.e. 5 cyclesidegree). The orientation and spatial position of local stimulus elements were varied during visual stimulation. On the top center and top right are shown reconstructed PETT data obtained following visual stimulation. The mid-line is indicated by a line, and a small region in the area of the identified primary visual cortex topographic signature is shown enclosed by a set of 4 boxes. The size of these boxes is 2 x 2 cm. The color scale used to pseudo-color the PETT data is the 'heat scale': twelve equal bins of data are displayed, using white, yellow, orange, red . . . blue for the pseudo-color display. Thus, the posterior region of primary visual cortex in the left hemisphere is stimulated (top center), corresponding to the superior central right visual field stimulation. This PETT section was located 4.5 cm above the cantho-meatal plane. In the higher section shown, located at 5.5 centimeters above the cantho-meatal plane, the pattern of [^{18}F]DG labeling has shifted forwards, to an anterior position (by about 2 cm), and was still lateralized to the left hemisphere, as shown on the top right. The asymmetries in these two sections were measured to be 10 and 40% for the central (foveal) and peripheral regions, respectively. Noticeable in this figure is the 'spillover' from left to right hemisphere in the central representation (center top). This 'spillover' largely accounted for the smaller value of asymmetry observed in the central representation of visual field. On the lower part of the top section, 3 figures are presented for the purpose of illustrating the expected 'signature' of the stimulus. On the bottom left is shown a medial view of human visual cortexI3. The striped area represents striate cortex, and the shaded area represents the 'signature' of the stimulus shown on the top left. Thus, the small superior central region of stimulus corresponds to the inferior posterior region shaded in yellow (bottom left), while the larger peripheral region corresponds to the superior anterior cortical region shaded in yellow. Also shown are two dotted lines, parallel to the cantho-meatal plane, 'which are separated by 1 cm. Bottom center and bottom right of the top section show two sections of human brain, at the approximate cantho-meatal level of the two PETT sections shown on top. A similar indication of the mid-line and a 2 × 2 set of 'boxes' which are /each 2 x 2 cm in size, is also shown. The shaded areas in these 'boxes' correspond to the expected signature of the stimulus, lateralized to the left hemisphere, with the central visual region mapped to the posterior, inferior cortical 'box', while the peripheral visual region is mapped to the superior cortical 'box'. These match the observed PETT data very well. Bottom: same as above, but another subject, and another stimulus condition. The left visual field is stimulated in the superior central and inferior peripheral regions. Corresponding PETT sections indicated neural activation in the appropriate regions, as illustrated in the figure.

task, which is difficult to perform consistently for the 20 min duration of stimulation used, provided some degree of control over the internal state of the subjects. Of 4 subjects tested, two could not perform this task to criterion (>80%) and were eliminated from further study. The majority of the subjects reported that the task required focused attention, and was difficult. Thus, some degree of control over subject 'set' was provided.

Subjects spent about 20 min rehearsing the stimulus letter identification task with the particular stimulus movie which they were to view during the experiment. Two movies were used: a right visual field stimulus with superior central and inferior peripheral visual field stimulation, and a left visual field stimulus, with inferior central and superior peripheral visual field stimulation (Fig. 1).These were shown in alternation to successive subjects. Following rehearsal, dark adapted subjects received 5 miC injections (i.v.) of [^{18}F]DG. Then, a 20 min stimulation period followed, during which the subjects viewed the movie and identified the random letter presentations.

Following visual stimulation, subjects were placed in the PETT-I11 scanner. Head alignment was performed with lasers fixed with respect to the scanner gantry. Then, a series of 9 serial PETT scans were obtained, parallel to the cantho-meatal (CM) plane, starting at 2–2.5 cm above the CM plane. Head position was monitored during scanning with the same laser system used for initial set-up. PETT sections were obtained at 0.8 cm intervals (0.5 cm for one subject) over a range of 5 cm, for a total of 7 male, adult (age 20–50 years) subjects.

Image analysis was performed off-line using a computer controlled (PDP-11/23) color video display system. The images obtained from each subject were visually examined for evidence of the expected 'signature' created by the stimulus movie. Examples of this expected 'signature', the stimulus, and representative PETT data, are shown in Fig. 1. The topographic signatures expected are clearly evident in Fig. 1, in the form of an asymmetry whose CM and anterior-posterior coordinates change in the manner predicted by the topographic structure of the stimulus.

The predicted pattern of topographic and lateralized cortical stimulation (Fig. 1)was located in 6 of 7 subjects, by visual inspection of computer graphic displays of the PETT data. Quantitative analyses of this data were performed by shifting a small grid composed of four 2 x 2 cm boxes (Fig. 1) along the midline of the sections in the PETT sections in which the topographic 'signature' was observed. Using estimates of striate cortex surface area in humansl3, and mathematical models of striate cortex topography [3,11,12] the cortical representation of the stimulus was expected to consist of 4 equal sized 'patches', corresponding in size to this grid. The midline of each PETT section was found by fitting a line to the average of the geometric limits of the PETT images at anterior, central, and posterior positions. Then, the grid (Fig. 1) was shifted along this mid-line in order to provide the best fit to the expected pattern of stimulation. When the optimal grid position was found, asymmetry was calculated by dividing the difference of the ipsilateral and contralateral [^{18}F]DG counts by their sum, in each box of the grid, for homologous areas on either side of the midline. The result of this analysis was that an average asymmetry of 15% (central) and 24% (peripheral) was found in the group of 6 subjects (see Table I).

The smaller asymmetry observed in the central (0–10°) representation of striate cortex was visually confirmed by examining the PETT data. Several of the subjects had a noticeable 'spillover' of FDG activity, in the central (but not peripheral) representation, from contralateral to ipsilateral hemispheres. The examples of data shown in Fig. 1indicates clearly this central 'spillover'effect.

The cause of this reduced asymmetry in the central

TABLE I

The asymmetries in the region of *VI*

Subject VS002 had no observable effect correlated to the stimulus (NOE) The asymmetries are calculated as described in the text.

Subject	***Central asymmetry***	***Peripheral asymmetry***
VS00l	11%	40%
VS002	NOE	NOE
VS003	14%	6%
VS004	29%	59%
VS005	20%	6%
VS007	12%	23%
VS009	4%	8%
Average	15%	24%

representation could be due to: (1) the bilateral presentation of the fixation letter; or (2) small errrors in eye fixation. Both of these effects would be exaggerated by the large value of cortical magnification in the central visual representation.

The topographically distributed asymmetries observed in the present experiment (15% central, 24% peripheral) may be compared with a previous experiment using PETT-III[5] which studied hemi-field stimulation, but not topographic mapping. The average asymmetry obtained in that experiment was 8%, which is similar to the central value obtained in the present experiment, but smaller than the peripheral value obtained in the present experiment. These differences may be due to the fact that the topographic aspect of the present experiment allowed a more accurate location of primary visual cortex, to the use of a cortical magnification factor scaled stimulus in the present experiment, or to differences in the eye fixation paradigms used in these experiments.

Another previous PETT experiment compared eyes-open to eyes-closed stimulus conditions, using a parafoveal checkerboard of constant size (1°). In this work, an increase in the metabolic activity of primary visual cortex of 28.8% was reported. Although the stimulus conditions and instrumentation in this experiments are not directly comparable to the present experiment, this amount of increased cortical metabolic activity is similar to the peripheral asymmetry observed in the present experiment.

In summary, the present work demonstrates that, despite the difficulties imposed by PETT technology, it is feasible to study patterns of topographic mapping in human primary visual cortex. In particular, the reasonably well understood topographic structure of primary visual cortex may be used, together with the lateralized representation of the visual field, to provide a 'signature' to verify the location of a specific architectonic area (i.e. striate cortex) in the PETI data. This is particularly important because of the complexity of the PETT images, the relative lack of experience in interpreting these images, and the difficulty in using independent means of verification (such as CAT scans) to locate specific cortical areas. This approach will be utilized with PETT-VI, which is a new scanner beginning to be used in our laboratory, which has about twice the spatial resolution of the PETT-I11 scanner used in the present experiment. It may be possible to obtain an approximate measurement of human cortical magnification factor by means of imaging a finer cortical 'checkerboard' pattern than the one used in the current experiment. Furthermore, the present work demonstrates that imaging cortical topography via PETT scanning provides a landmark in the visual system of individual subjects. Since a reasonable amount of variation in location of primary visual cortex was expected, and observed in the present experiment (on the order of 1–2 cm), it would seem that in order to study the stimulus preferences of human visual cortex, some form of anatomical verification is necessary. The topographic 'signature' observed in the present experiment provides one such verification.

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