GRAPHICAL ANALYSIS OF REGIONAL BLOOD FLOW DISTRIBUTION BY MEANS OF PSEUDOCOLOR ORGAN MAPS

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Regional organ blood flow can be measured by means of radioactive microspheres with a spatial resolution of approximately 50-100mg [1,4]. Encoding the blood flow values as pseudocolors allows to display the blood flow distribution in organ surfaces or cross-sections in organ flow 'maps'. Pseudocolor mapping is helpful in the descriptive assessment of blood flow heterogeneity and changes over time as well as for identification of flow patterns. This technique was reported for the heart using gray scale shading [4] or drawing patterns [7,8]. We have used the SAS statistical software package (SAS/BASE, SAS/GRAPH, Version 5.16 and 5.18) for VAX/VMS in order to realize a general application program package that can produce maps not only from the heart but from any user defined organ map. Blood flow data may be encoded by using gray scale shading, color lookup tables or drawing patterns.

Material and Methods

Experimental Data

The data used to illustrate this study were obtained from two series of experiments in dogs. Series I was designed to assess the methodological error of the microsphere method (3 animals). From series I, the lung data are used. Series II was performed in order to study the effect of pulmonary hypertension and PEEP ventilation (positive end-exspiratory pressure) on regional blood flow in various organs. From series II, the heart data are used.

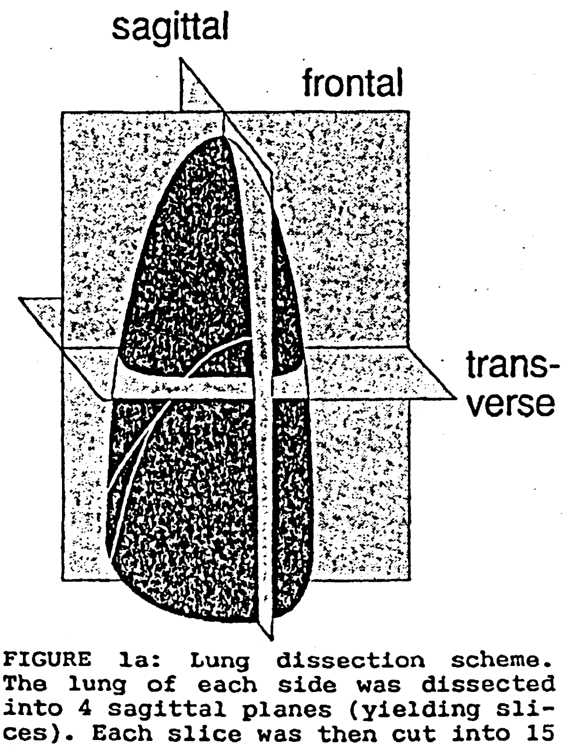


FIGURE 1a: Lung dissection scheme. The lung of each side was dissected into 4 sagittal planes (yielding slices). Each slice was then cut into 15 transverse planes (yielding stripes), and each stripe was subdivided into 10 frontal planes (yielding samples). Grid size was 2 cm for all planes. Depending on the individual size of the lungs, 300-400 samples were obtained from one animal.

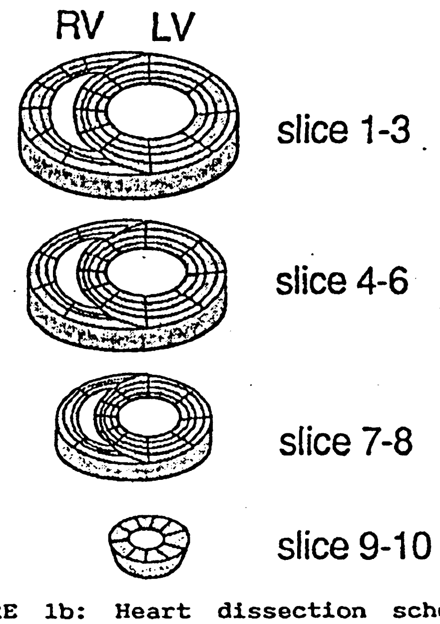


FIGURE 1b: Heart dissection scheme (atria removed). Each heart was dissected into 10 slices perpendicular to its axis. Slices 1-8 were subdivided into right (RV) and left ventricle (LV). The LV was dissected into 10 segments, and the RV into 7 (slice 1-3), 5 (slice 4-6) or 3 se- ments (slic segments we 3 (RV) lay results in (126 RV sam

Radioactive Microsphere Technique

Briefly, the technique is based on the entrapment of small plastic beads (15μ) in the capillary network of the circulation. Repeated injections of particles labeled with different nuclides yield consecutive 'snapshots' of blood flow in the temporal dimension. After dissection of the organ(s) and counting of sample radioactivities, blood flows can be calculated for each sample and each injection. Further details have been described elsewhere [3].

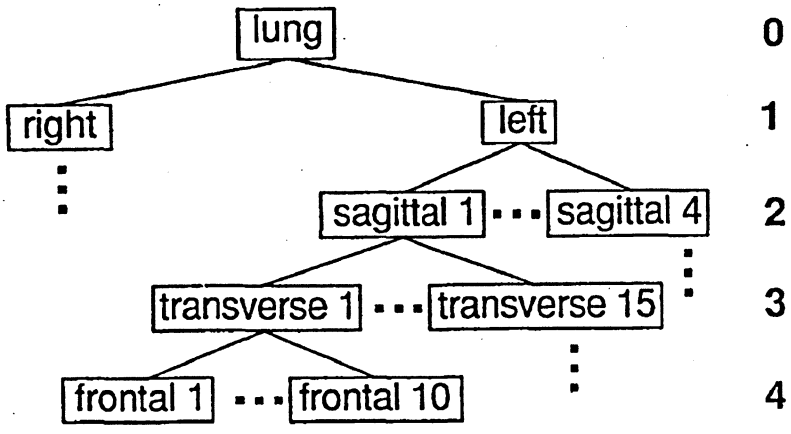


FIGURE 2a: Hierarchical dissection tree of the lung (represents scheme of Fig. 1a). The tree has 5 levels (root level 0, node levels 1-4), and only 1 branch is shown completely (left lung, sagittal 1, transverse 1 and frontal 1).

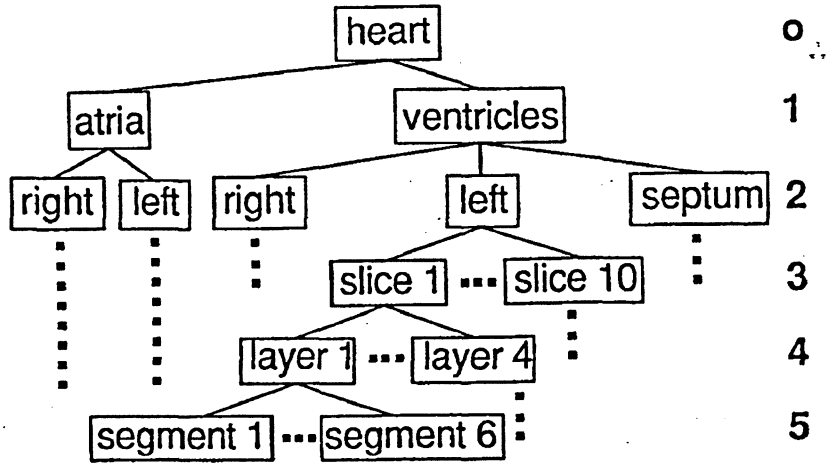


FIGURE 2b: Hierarchical dissection tree of the heart (represents scheme of Fig. 1b). The tree has 6 levels (root level 0, node levels 1-5), and only one branch is completely shown (left ventricle, slice 1, layer 1 and segment 1). Other branches are constructed in the same manner.

Organisation of the data

The samples are counted in a gammaspectrometer [6]. After the spectra have been unfolded, the data are transferred in ASCII format via DECnet from the gammaspectrometry computer (formerly PDP11/24, now VAX11/730) to a MicroVAX II on which the analysis is carried out. The data are organized in a rectangular file structure. Each sample is identified by the numbers of experiment and injection as well as by classification variables that represent the dissection tree.

Fig. 1a shows the dissection scheme of the lung (series I). Fig. 1b illustrates the dissection scheme of the heart (series II). The dissection tree and its hierarchical structure are explained for the lung (Fig. 2a) and heart (Fig. 2b) schemes. Fig. 3 indicates the organisation of the SAS permanent data set after the ASCII files have been processed and blood flows have been calculated.

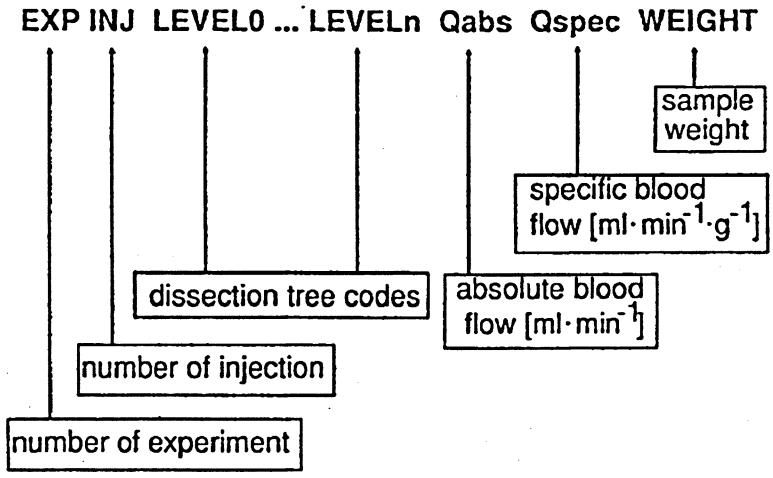


FIGURE 3: Data set structure. In the rectangular file, each blood flow value is identified by number of experiment, number of injection, and dissection tree codes. Data to be kept for analysis are absolute and specific blood flow, and sample weight.

User-defined map data sets

Several map data sets have been created, e.g. for heart, kidney, lung, brain, and intestinal organs. The maps of heart and kidney were generated by using circle, ellipsis and linear equations. More complex maps, e.g. of brain and intestinal organs, were obtained from digitizing suitable drawings. Fig. 4 explains how user defined map data sets are created by digitizing. Further details are described elsewhere (SAS TR A-107).

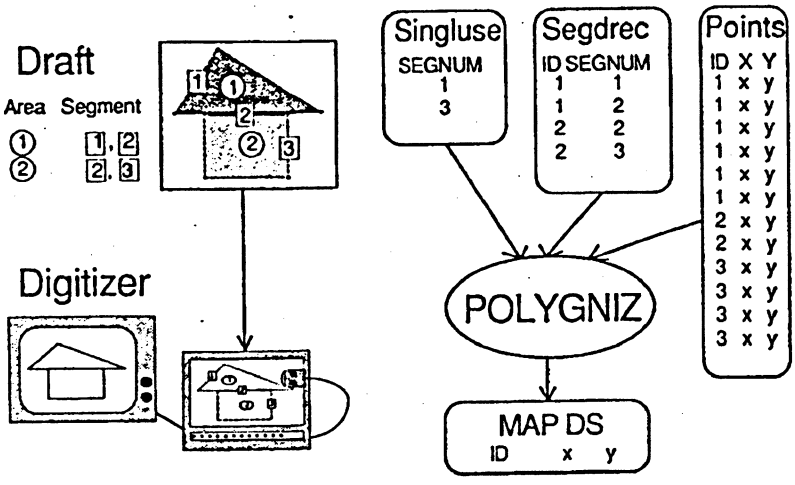


FIGURE 4: Creating user-defined maps. a) DRAFT: The user has to break down the object into areas and segments (polygons enclosing the areas). The segments are distingished into single used (belonging to one area) and multiple used polygons (belonging to two adjacent areas). b) DIGITIZING: For each digitized segment, an ID code must be provided. c) MAP DATA SET: From user-provided tables SINGLUSE (directory of single used segments) and SEGDREC (directory of areas and their enclosing segments), and from the file POINTS (digitized coordinates), the program POLYGNIZE creates a map data set (cf. SAS technical report TR A-107).

User-written SAS Application Programs

A standard procedure for the type of maps that is needed for blood flow analysis is not available from SAS. Thus customized application programs using PROC and DATA steps were designed. The principle construction of these programs is shown in Fig. 5. The user sees only the declaration part, while the SAS programs are linked by %INCLUDE during execution. Fig. 6 gives an overview of the declarations that the user has to provide in the declaration program. The parameter declarations are assigned to global Macro variables by %LET. At present, two application programs are available, the programs 'LAYOUT' and 'PLOT'.

- ▸LIBNAMEs, FILENAMEs
- ▸Permanent Data Sets, GSFNAME
- ▸BY varlists
- ▸Control of graphic contents
- ▸Control of graphic layout
- ▸Control of driver (options)

FIGURE 5: Parameters defined in the declaration program.

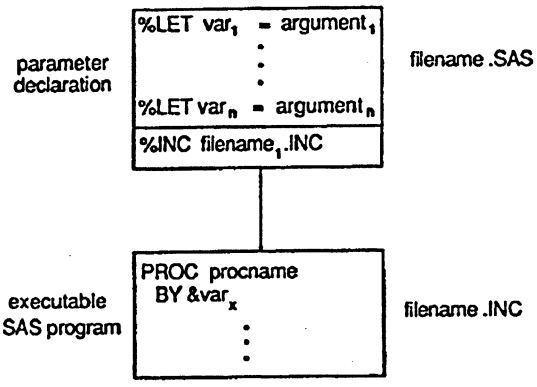
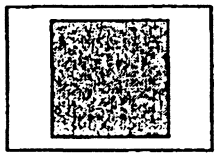
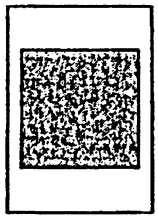


FIGURE 6: Principle design of program 'LAYOUT' and 'PLOT'. Using a small SAS frame program that is annotated with comments and explanations, the user assigns his particular parameter values to Macro variables (%LET=) and stores the frame program under a new file name. On execution of this declaration program, the SAS program is linked (%INCLUDE). From the user's view, only the program that processes his data is 'executable'.

Application program 'LAYOUT'

The main purpose of the program 'LAYOUT' is to create a customized map data set with standard scaling x=(0,100) and y=(0,100) in which several original maps, e.g. of organ cross-sections, can be arranged as needed. The orginal maps, which can have any scaling of coordinates, may be rotated and translated as requested by the user. The program 'LAYOUT' divides the plotting area into pseudo-templates, the form of which can be selected by the user (Fig. 7). The original maps are then fitted into these pseudo-templates. Figs. 8a and 8b show two typical applications of 'LAYOUT', namely the arrangement of several cross-sectional maps (used for analysis of blood flow in several regions at the same time), and the reduplication of one cross-sectional map with a new ID variable, e.g. INJ to allow plotting of blood flows obtained from repeated injections (used for analysis of several measurements of one region).


landscape


portrait

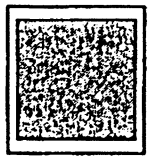

'best'

FIGURE 7: Fitting actual maps int pseudo templates (program 'LAYOUT'; Options are 'landscape', 'portrait and 'best'.

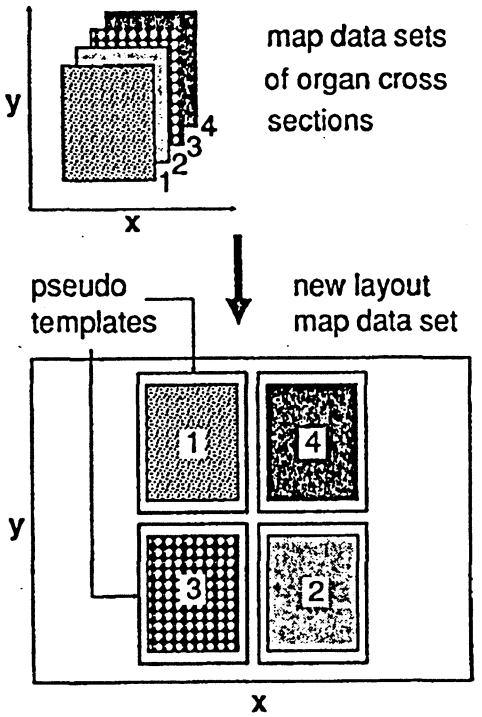


FIGURE 8a: Creating customized map data sets (program 'LAYOUT'). Maps of several cross-sections are arranged as needed in the plotting area of x=(0,100) and y=(0,100).

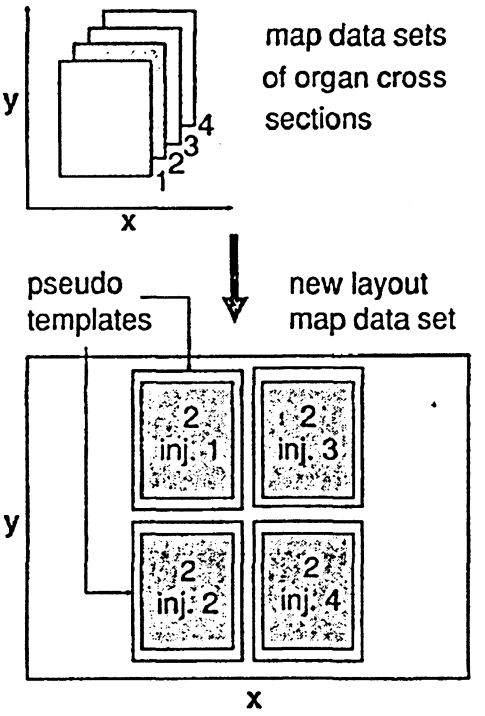


FIGURE 8b: Creating customized map data sets (program 'LAYOUT'). One map is replicated several times and arranged in the plotting area of x=(0,100) and y=(0,100). An additional ID variable (e.g. INJ) is appended.

Application program 'PLOT'

In a second step, the map data set created by 'LAYOUT' is input into the application program 'PLOT' together with the response data set (blood flow data) and an ASCII file that contains the color coding of the lookup table. Any valid SAS color system (RGB, HLS and GRAY) can be used. SAS patterns for plotter output are also supported. The principle design of 'PLOT' is depicted in Fig. 9. 'PLOT' produces two plots, the organ map and the lookup table along with a title. Both plots are put together into a standard template as shown in Fig. 10.

We use the glow scale color lookup table, which has been validated [2] and is routinely used in radiology [5]. The glow scale shows the color changes of a black body during continous heating, i.e. from black to red, orange, yellow and white. Depending on the number of colors supported by the output device, the lookup table is divided into 10-12 (VT340 graphic terminal) up to 128 distinct colors (HP7510 film recorder). Other devices drivers that can be used with 'PLOT' are PS300 (Dataline 1260 PostScript laser printer) and HP7550A (Canon LBP 8 A2 laser printer). The lookup table for the PS300 device driver consists of 8 distinct gray levels, and the lookup table for the HP7550A driver simulates 6 gray shades by appropriate patterns.

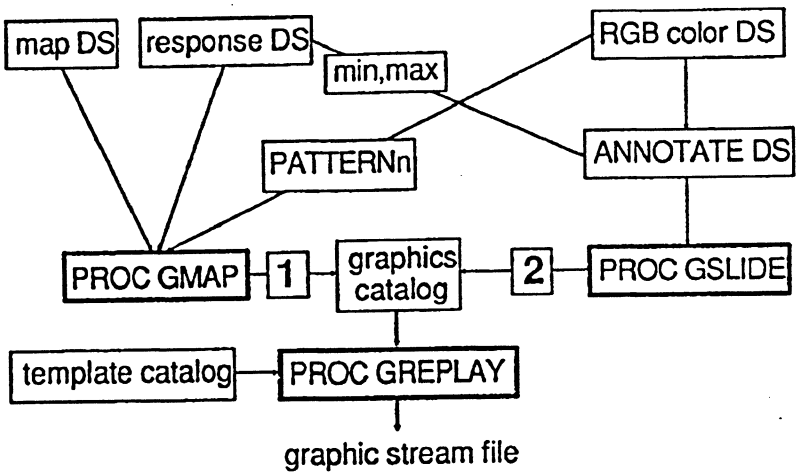


FIGURE 9: Structure of program 'PLOT'. Imported are the map and response data sets, and the lookup table data set (e.g. RGB). From the response data set, the user-selected minima and maxima of blood flows (e.g. P5 and P95) are calculated. They are used to label the lookup table (by ANNOTATE) and to calculate the MIDPOINTS for PROC GMAP. PATTERN statements are created from the lookup table data set. PROC GMAP produces the organ map (plot 1), and PROC GSLIDE builds the lookup table and title (plot 2). Finally, both plots are linked by PROC GREPLAY and a GSF file is produced.

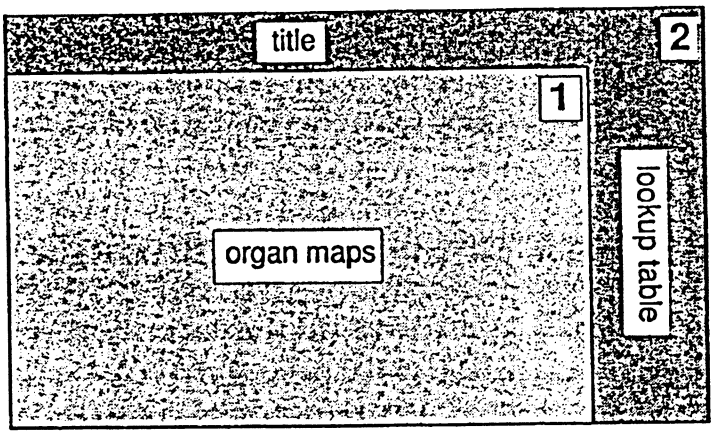


FIGURE 10: Templates used by program 'PLOT'.

Applications

Fig. 11 shows blood flow mapping of the lung in normal anesthetized dogs in left lateral position. Eight sagittal cross-sections are depicted. Obviously, there is a flow gradient from the core of the lung (high flow) to the peripheral shell (low flow). The left lung is not greatly different from the right lung, thus gravitational force is of minor influence.

Fig. 12 shows the change of blood flow in the dog heart after induction of pulmonary hypertension (infusion of glass beads) and subsequent ventilation with PEEP (positive end-expiratory pressure). There is a continous increase of blood flow that is most pronounced in the inner (endocardial) layers of the right ventricle.

Problems encountered with SAS

All problems relate to SAS/GRAPH. There is a known trouble between the SAS device driver and the VT340 graphic terminal hardware. A set of coordinates, that produces a circle e.g. on the HP7550A plotter, is displayed as an ellipsis on the VT340. We found empirically, that compression by 0.92 (x) and 0.98 (y) for the VT340 gives approximate equal circles on both devices.

On the HP7510 film recorder, a green value of 128 (decimal) produces blackish green that is hardly to distingu[illegible]
colors are fairly in agreement with thei[illegible]
ble to problems of the SAS HP7510 driver.

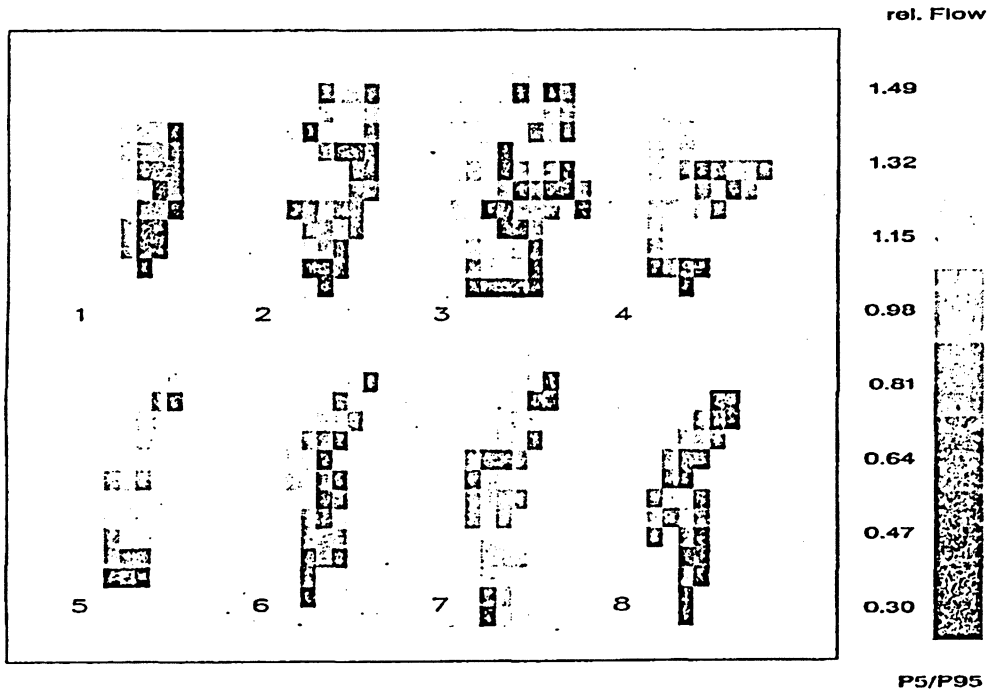


FIGURE 11: Organ maps of the lung, sagittal cross-sections. From series I, experiment 2, pulmonary injection of microspheres. The lookup table ranges from P5 to P95. Blood flows are expressed as relative flows (normalized with respect to the mean of all blood flow values contributing to the graph). Device was Dataline 1260 laser printer, driver was PS300).

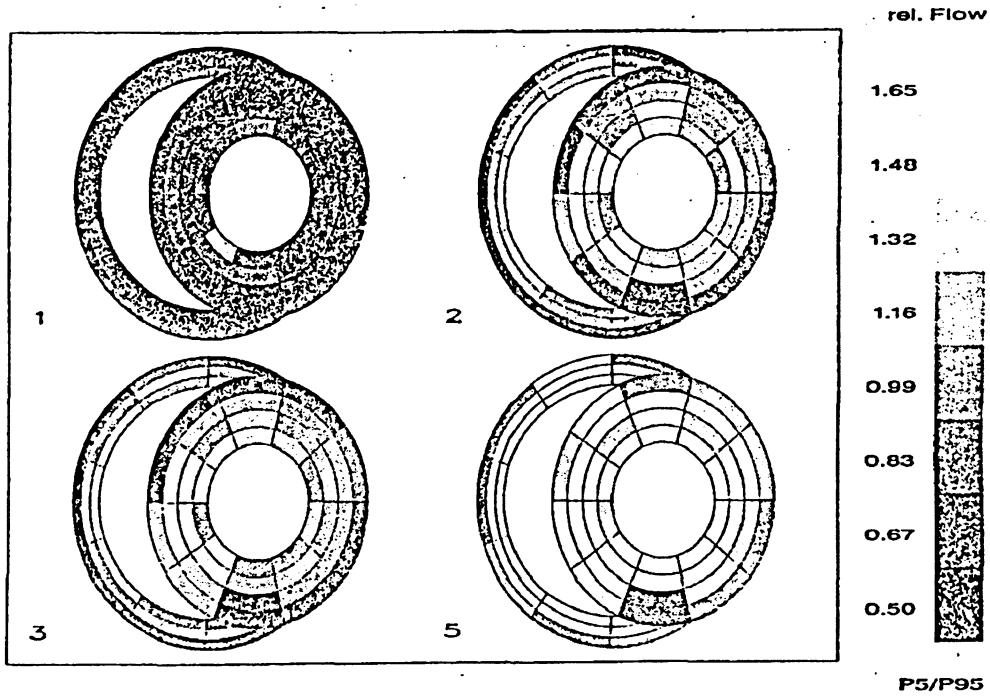


FIGURE 12: Organ maps of the heart, slice 3. From series II, experiment control measurement (inj. 1), pulmonary hypertension (inj. 2), PEEP 10 (in 3) and PEEP 20 (inj. 5). The lookup tabl
are expressed as relative flows (normali
blood flow values contributing to the gr
printer, driver was PS300).

Using the glow scale on the HP7510 film recorder, colors are arbitrarily remapped in such a way that a yellow tone appears amidst the area of dark red, and red appears on the blackish end of the lookup table. Remapping of this type occurs no matter how many colors are used for the lookup table (16, 32, 64, 128). We were not able, to locate the problem, but we suspect that it occurs either in PROC GREPLAY or in the HP7510 driver.

Another type of unpredictable color remapping was encountered if the colors of CBACK= (in GOPTIONS) and CEMPTY= (in PROC GMAP) are equal and of the same color system. The error is not occurring, if the colors are specified by using different systems, say CXFFFFFF and GRAYFF (both produce white). This bug could be clearly located in PROC GREPLAY by using the VT340 color setup feature. After the output of PROC GREPLAY has been displayed, the CEMPTY= color has been written into location 13 of the VT340 color lookup table, while location 0 shows black (standard background color). After PROC GREPLAY has processed the output of PROC GMAP (from the graphics catalog) into a template (from a template catalog) and has displayed the graph on the VT340, the colors in locations 0 and 13 are exchanged and empty areas are outlined in black, while the background color is correct.

Another problem in our application was associated with the extensive autoscaling features of PROC GMAP. In an attempt to fill the plotting area as much as possible, PROC GREPLAY rescales the map data set and hereby distorts the shape of the objects. This could only be circumvented by adding two small dummy areas to the map data set, one in the left lower corner (0,0) and the other in the upper right corner (100,100) of the map produced from program 'LAYOUT'.

A device-dependent problem is that the HP7510 film recorder produces fairly thick lines that may overwrite the color of small areas. Therefore, a line width option for CEMPTY= and COUTLINE= of PROC GMAP would be desirably.

Conclusions

The application programs 'LAYOUT' and 'PLOT' have been designed with the aim of giving unexperienced users a tool at hand that allows to produce complex pseudocolor organ maps without having indepth experience with SAS/GRAPH. Once the layout of the maps has been worked out, routine production of organ flow maps can be quickly accomplished by the program 'PLOT'. The organ flow maps have proved to be a valuable tool for exploratory data analysis of regional blood flow distribution, in particular for the detection of flow patterns and changes. Since both programs have been implemented in SAS, they are available on a variety of computers, and thus to a large community of researchers using the microsphere technique.

Acknowledgement: The generation of appropriate RGB values for the glow scale was adopted from a FORTRAN routine that was provided by Dr. Schlegel, German Center for Cancer Research, Im Neuenheimer Feld 280, D-6900 Heidelberg, FRG

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