Method Article

Semi-automated segmentation of the lateral periventricular regions using diffusion magnetic resonance imaging

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Abstract

The lateral ventricular perimeter (LVP) of the brain is a critical region because in addition to housing neural stem cells required for brain development, it facilitates cerebrospinal fluid (CSF) bulk flow and functions as a blood-CSF barrier to protect periventricular white matter (PVWM) and other adjacent regions from injurious toxins. LVP injury is common, particularly among preterm infants who sustain intraventricular hemorrhage or post hemorrhagic hydrocephalus and has been associated with poor neurological outcomes. Assessment of the LVP with diffusion MRI has been challenging, primarily due to issues with partial volume artifacts since the LVP region is in close proximity to CSF and other structures of varying signal intensities that may be inadvertently included in LVP segmentation.

This research method presents:

- A novel MATLAB-based method to segment a homogenous LVP layer using high spatial resolution parameters (voxel size $1.2 \times 1.2 \times 1.2$ mm$^3$) to only capture the innermost layer of the LVP.
- The segmented LVP is averaged from three contiguous axial slices to increase signal to noise ratio and reduce the effect of any residual volume averaging effect and eliminates manual and inter/intrarater-related errors.

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Specifications table

| Subject Area                           | Neuroscience                                      |
|----------------------------------------|--------------------------------------------------|
| Method name:                           | Segmentation of lateral ventricular perimeter regions of interest |
| More specific subject area             | Image processing for brain diffusion MRI         |
| Name and reference of original method  | N/A                                              |
| Resource availability                  | 1. MATLAB (https://www.mathworks.com/products/matlab.html) |
|                                        | 2. The tilefigs.m program, previously described by Charles Plum [2] was used only to display images already created by the algorithm (https://www.mathworks.com/matlabcentral/fileexchange/328-tilefigs-m). |

Method details

The semi-automated algorithm for selecting periventricular ROIs begins by reading standard processed DTI files into MATLAB. Images showing mean diffusivity (MD) are displayed sequentially to allow the user to select slices centered on the foramen of Monro. Once this slice is determined, the algorithm automatically selects three total axial slices (one rostral and one caudal to the center slice) for further analysis. The MD image is used since it provides a sharp demarcation between the brain parenchyma and the CSF.

The script then displays a histogram of the MD values present in the center slice, which appears as a bimodal distribution. The lower peak of this distribution represents MD values in the brain parenchyma, and the higher peak represents the cerebrospinal fluid spaces. Based on this histogram, the user determines a threshold value that best separates parenchyma and CSF MD values. Following this, the script produces an image showing voxels with MD values above the threshold. When properly executed, these steps result in a few predominant regions representing the lateral and third ventricles, along with some small peripheral regions of CSF. Through sequential erode and dilate steps, the selected regions are smoothed, and small extraneous spaces are removed.

Next, the script calculates the number of objects in each slice and the area of each object (blob analysis) and displays this information. A predetermined minimum size (we used 10 voxels) is applied to display only areas that are likely to be involved in the ventricular system. The script also determines the center of mass of each object, with the assumption that true ventricular objects will be close to the center of the brain. At this stage, the user selects the number of objects to be further processed, which should include all objects that represent ventricular spaces. The script produces an image of all objects that are greater than the minimum size, and the user is able to click near the center of mass of each object to be included in the final selection. Once the relevant objects are selected, the script saves those selections and removes extraneous objects from further analysis. This process is repeated for each of the three contiguous slices.

After the ventricular spaces have been selected, the script isolates the periventricular voxels. This is done by performing two sequential dilation steps, incorporating voxels that are one and two spaces away from the ventricles and then subtracting the original ventricle objects from the dilated objects. The final periventricular ROI is then saved, and it can be sampled for individual DTI parameters.
The anterior (frontal) and posterior (occipital) horns of the lateral ventricle may be independently segmented. In order to select only the frontal and occipital horns, the previously segmented “full” periventricular objects are further modified as follows.

- The center point of the periventricular ROIs in the anterior-posterior (A-P) direction is calculated. This divides the brain into an anterior and posterior segment.
- The script then locates the most anterior and most posterior voxels that are also included in the ROI. This identifies the most anterior and posterior aspects of the ventricles which are then used to select all voxels that are within a predetermined A-P distance from these most extreme points for inclusion in the frontal and occipital horn perimeters.
- An additional step separates the left frontal, right frontal, left occipital, and right occipital objects for individual analysis.

**Step-by-step guide**

All MATLAB scripts required to run the program is included here. To run the program effectively, and to avoid bugs, we recommend the folder/file structure outlined on Supplementary Fig. 1. Should the user decide to use our recommended structure, all the dMRI images to be analyzed may be placed into folders separated by their **“Study Groups”**. The following MATLAB scripts can then be used as is to create the 12 files in the “Codes” folder, which are all required for parsing the LVP (“full”) and frontal-occipital horn (“corners”) regions.

| 1 | add_moments.m |
| --- | --- |
| % add new pixel to existing blob |
| function [blob1, bimg] = add_moments(bimg,i,nblob,blob1,nx) |
| x = mod((i-1),nx)+1; |
| y = floor((i-1)/nx)+1; |
| z = 0; |
| bimg(i) = nblob; |
| blob1.m000 = blob1.m000 + 1; |
| blob1.m100 = blob1.m100 + x; |
| blob1.m010 = blob1.m010 + y; |
| blob1.m001 = blob1.m001 + z; |
| blob1.m110 = blob1.m110 + x*y; |
| blob1.m101 = blob1.m101 + x*z; |
| blob1.m011 = blob1.m011 + y*z; |
| blob1.m200 = blob1.m200 + x^2; |
| blob1.m020 = blob1.m020 + y^2; |
| blob1.m002 = blob1.m002 + z^2; |
| Return |
bindilate.m

function [out2d] = bindilate(img2d, N)

[nx, ny] = size(img2d);
out2d = zeros(nx, ny);
for i = 2:nx-1
   for j = 2:ny-1
      if img2d(i,j)==1
         out2d(i,j) = 1;
         continue
      end
      sum = img2d(i-1,j-1) + img2d(i-1,j) + img2d(i-1,j+1)+ ...
            img2d(i,j-1) + img2d(i,j+1)+ ...
            img2d(i+1,j-1) + img2d(i+1,j) + img2d(i+1,j+1);
      if sum >= N
         out2d(i,j) = 1;
      else
         out2d(i,j) = 0;
      end
   end
end

binerode.m

function [out2d] = binerode(img2d, N)

[nx, ny] = size(img2d);
out2d = zeros(nx, ny);
for i = 2:nx-1
   for j = 2:ny-1
      if img2d(i,j)==0
         out2d(i,j) = 0;
         continue
      end
      sum = img2d(i-1,j-1) + img2d(i-1,j) + img2d(i-1,j+1)+ ...
            img2d(i,j-1) + img2d(i,j+1)+ ...
            img2d(i+1,j-1) + img2d(i+1,j) + img2d(i+1,j+1);
      if 8-sum >= N
         out2d(i,j) = 0;
      else
         out2d(i,j) = 1;
      end
   end
end
return
calc_blobs.m

% calc_blobs
% convert from raw blobs to real blobs
% keep only objects with area > area_min
% nblob: is the final number of raw blobs
% lub: look up blob, table to point from raw blob to new blob number
% nobj: number of real blobs

function [nobj, lub, obj] = calc_blobs(blob, area_min, adj_reg, parents, lub, blob, obj);

nobj = 0;

for i = 1:nblob
    if adj_reg(i) == 0
        continue
    end
    lub(i) = i;
    next = adj_reg(i);
    while (next > 0)
        blob(i).m000 = blob(i).m000 + blob(next).m000;
        blob(i).m001 = blob(i).m001 + blob(next).m001;
        blob(i).m010 = blob(i).m010 + blob(next).m010;
        blob(i).m100 = blob(i).m100 + blob(next).m100;
        blob(i).m011 = blob(i).m011 + blob(next).m011;
        blob(i).m101 = blob(i).m101 + blob(next).m101;
        blob(i).m110 = blob(i).m110 + blob(next).m110;
        blob(i).m200 = blob(i).m200 + blob(next).m200;
        blob(i).m020 = blob(i).m020 + blob(next).m020;
        blob(i).m202 = blob(i).m202 + blob(next).m202;
        tmp = adj_reg(next);
        lub(next) = i;
        adj_reg(next) = 0;
    end
    for j = 1:nblob
        if parents(j) == next
            parents(j) = i;
        end
    end
    next = tmp;
end

if blob(i).fgflg == 1 & blob(i).m000 >= area_min
    nobj = nobj + 1;
    obj(nobj).fgflg = 1;
    obj(nobj).xbeg = blob(i).xbeg;
    obj(nobj).ybeg = blob(i).ybeg;
    obj(nobj).xend = blob(i).xend;
    obj(nobj).yend = blob(i).yend;
    obj(nobj).m000 = blob(i).m000;
    obj(nobj).m001 = blob(i).m001;
    obj(nobj).m010 = blob(i).m010;
    obj(nobj).m011 = blob(i).m011;
    obj(nobj).m100 = blob(i).m100;
    obj(nobj).m101 = blob(i).m101;
    obj(nobj).m110 = blob(i).m110;
    obj(nobj).m200 = blob(i).m200;
    obj(nobj).m020 = blob(i).m020;
    obj(nobj).m202 = blob(i).m202;
end

return

connect_reg.m

% connect_reg
% make note of blobs that are connected
% input n,m of the two blobs to be connected
% make change in adj_reg array to track this info

function [adj_reg] = connect_reg(adj_reg, n, m)

tmp = adj_reg(n);
while (tmp == m)
    if tmp == m
        return
    end
    tmp = adj_reg(tmp);
end

tmp = adj_reg(n);
adj_reg(n) = adj_reg(m);
adj_reg(m) = tmp;
return
```matlab
function img_out = corners(img, limnum, Nx, Ny, select)

    img_out = img;
    Nxhalf = floor(Nx/2);

    % first hemisphere
    ymax = Ny/2 + limnum;
    ymin = Ny/2 - limnum;

    for p = 1:Nxhalf
        for q = 1:Ny
            if img(p,q)==0
                continue
            end
            if q > ymax
                ymax = q;
            end
            if q < ymin
                ymin = q;
            end
        end
    end

    for p = 1:Nxhalf
        for q = 1:Ny
            if img(p,q)==0
                continue
            end
            if ismember(select,[1 3])
                img_out(p,q)=0;
            elseif ymax - q >= limnum && q - ymin >= limnum && select==5
                img_out(p,q)=0;
            elseif q - ymin >= limnum && select==2
                img_out(p,q)=0;
            elseif ymax - q >= limnum && select==4
                img_out(p,q)=0;
            end
        end
    end

    % second hemisphere
    ymax = Ny/2 + limnum;
    ymin = Ny/2 - limnum;

    for p = (Nxhalf+1):Nx
        for q = 1:Ny
            if img(p,q)==0
                continue
            end
            if q > ymax
                ymax = q;
            end
            if q < ymin
                ymin = q;
            end
        end
    end
```
end

for p = (Nxhalf+1):Nx
    for q = 1:Ny
        if img(p,q)==0
            continue
        end

        if ismember(select,[2 4])
            img_out(p,q)=0;
        elseif ymax - q >= limnum & & q - ymin >= limnum & & select==5
            img_out(p,q)=0;
        elseif q - ymin >= limnum & & select==1
            img_out(p,q)=0;
        elseif ymax - q >= limnum & & select==3
            img_out(p,q)=0;
        end
    end
end

end

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find_blob.m

% blob finding routine
% searches input img2d in column order
% keeps only foreground blobs with area greater than areamin
% returns the number of objects, critical values on objects
% and final image

function [nobj, objval, out2d] = find_blob(areaamin, img2d)

[nx, ny] = size(img2d);
out1d = zeros(1, nx*ny); % output 1d
out2d = zeros(nx,ny); % output 2d

Maxblob = 500;
oneblob = zeros(1,1);
adj_reg = zeros(1,Maxblob);
parents = zeros(1,Maxblob);

blob = struct('fgflg', initblob, ...
    'm000', initblob, 'nblob', initblob, 'parent', initblob, ...
    'xbeg', initblob, 'ybeg', initblob, 'zbeg', initblob, ...
    'm100', initblob, 'm010', initblob, 'm001', initblob, ...
    'm110', initblob, 'm101', initblob, 'm011', initblob, ...
    'm200', initblob, 'm020', initblob, 'm002', initblob);

blob1 = struct('fgflg', oneblob, ...
    'm000', initblob, 'nblob', initblob, 'parent', initblob, ...
    'xbeg', oneblob, 'ybeg', oneblob, 'zbeg', oneblob, ...
    'm100', oneblob, 'm010', oneblob, 'm001', oneblob, ...
    'm110', oneblob, 'm101', oneblob, 'm011', oneblob, ...
    'm200', oneblob, 'm020', oneblob, 'm002', oneblob);

objs = struct('fgflg', initblob, ...
    'm000', initblob, 'nblob', initblob, 'parent', initblob, ...
    'xbeg', initblob, 'ybeg', initblob, 'zbeg', initblob, ...
    'm100', initblob, 'm010', initblob, 'm001', initblob, ...
    'm110', initblob, 'm101', initblob, 'm011', initblob, ...
% open file
bimg = reshape(img2d,[1,nx*ny]);

% background blob starts with 1
nblob = 0;

% create frame as bg area in 1st blob
[nblob, blob(nblob), bimg] = init_moments(1,nx,0,0,nblob,blob1,bimg);

% blob(nblob) = blob1;
adj_reg(nblob) = nblob;
parents(nblob) = 0; % parent of main bg is zero

% fill first column as bg
for i = 1:nx+1
   bimg(i) = nblob;
end

% loop over image
for i = nx+2:nx*ny-1
   ba = i - nx + 1;
   bb = i - nx;
   bc = i - nx - 1;
   bd = i - 1;
   be = i + 1;

   % test patch of the array
   fprintf('%4d: %4d
',i,ba);
   fprintf('%4d %4d %4d %4d
',ba,bb,bc,bd);
   if nblob >= Maxblob
      fprintf('Error: number of raw blobs too large
');
      return
   end
   if bimg(i) == 1 % fg
      if blob(bimg(ba)), fgflag == 1
         [blob(bimg(ba)), bimg] = add_moments(bimg,i,bimg(ba),blob(bimg(ba)),nx);
      elseif blob(bimg(bd)).fgflag == 1 && & bimg(ba) == bimg(bd)
         adj_reg = connect_reg(adj_reg,bimg(ba),bimg(bd));
      else
         blob(bimg(ba)).fgflag == 1 && & bimg(ba) == bimg(bc)
         adj_reg = connect_reg(adj_reg,bimg(ba),bimg(bc));
      end
   else
      blob(bimg(bb)).fgflag == 1
      [blob(bimg(bb)), bimg] = add_moments(bimg,i,bimg(bb),blob(bimg(bb)),nx);
   else
      blob(bimg(bc)).fgflag == 1
      [blob(bimg(bc)), bimg] = add_moments(bimg,i,bimg(bc),blob(bimg(bc)),nx);
   else
      blob(bimg(bd)).fgflag == 1
      [blob(bimg(bd)), bimg] = add_moments(bimg,i,bimg(bd),blob(bimg(bd)),nx);
   else
      [nblob, blob1, bimg] = init_moments(1,nx,1,bimg(bd),nblob,blob1,bimg);
      blob(nblob) = blob1;
      adj_reg(nblob) = nblob;
      parents(nblob) = bimg(bd);
   end
   if blob(bimg(bb)).fgflag == 0
[blob(bimg(bb)), bimg] = add_moments(blob,bimg(bb),blob(bimg(bb)),nx);
if blob(blob(bimg(bb)),fgflg==0 && bimg(bb)==bimg(bb)
    adj_reg = connect_reg(adj_reg,bimg(bb),bimg(bb));
end
elseif blob(blob(bimg(bb)).fgflg==0
    [blob(blob(bimg(bb)), bimg] = add_moments(blob,bimg(bb),blob(blob(bimg(bb)),nx);
elseif blob(blob(bimg(bb))).fgflg==0 && bimg(be)==0
    [blob(blob(bimg(bb)), bimg] = add_moments(blob,bimg(bb),blob(blob(bimg(bb)),nx);
else
    [nblob, blobl, bimg] = init_moments(i,nx,0,bimg(bb),nblob,blobl,bimg);
    blob(nblob) = blobl;
    adj_reg(nblob) = nblob;
    parents(nblob) = bimg(bb);
end
end
% for j = 1:nblob
% fprintf('%d blob %d: adj_reg %d parents %d fgflg %d area %d n\n', ...
%        j,adj_reg(j),parents(j),blob(j).fgflg,blob(j).m000);
% end

nobj = 0;
out2d = reshape(blob, [nx,ny]);
% figure
% imshow(out2d, []);

% print out raw blobs
% for i = 1:nblob
% fprintf('%d blob %d: adj_reg %d parents %d fgflg %d area %d n\n', ...
%        i,adj_reg(i),parents(i),blob(i).fgflg,blob(i).m000);
% end

% lub = look up blobs, converts from raw blobs to final blobs
lub = zeros(1,nblob+1);
% areamin is input
[nobj, lub, objs] = calc_blobs(nblob,areamin,adj_reg,parents,lub,blob,objs);

% return critical values of:
% 1 blob number, 2 area,
% 3 x center, 4 y center
% 5 sum x2, 6 sum y2 around center, 7 xy around center
objval = zeros(7,nobj);
for i = 1:nobj
    objval(1,i) = objs(i).nblob;
    objval(2,i) = objs(i).m000;
    objval(3,i) = objs(i).m100/objs(i).m000;
    objval(4,i) = objs(i).m010/objs(i).m000;
    objval(5,i) = objs(i).m200/objs(i).m000 - objval(3,i)*2;
    objval(6,i) = objs(i).m020/objs(i).m000 - objval(4,i)*2;
    objval(7,i) = objs(i).m110/objs(i).m000 - objval(3,i)*objval(4,i);
end

% for i = 1:nblob+1
8 ImgDisp.m

function ImgDisp(img, tcs, slicelo, slicehi, mag, colorflag, imgtitle)

    [Nx Ny Nz] = size(img);

    imgvec = reshape(img, [1 numel(img)]);

    mag = floor(mag);

    % error checking
    if mag==0
        fprintf('Error(ImgDisp): mag cannot be zero');
        return
    end

    % get new dimensions and displacements in fft array
    Nxp = floor(mag*Nx);
    Nyp = floor(mag*Ny);
    Nxd = floor(0.5*Nx*(mag-1));
    Nyd = floor(0.5*Ny*(mag-1));

    Fimg = complex(zeros(Nxp, Nyp), zeros(Nxp, Nyp));
    Limg  = zeros(mag*[Nz Ny]);

    if strcmp(tcs,'tra')
        if mag==1
            for n = slicelo:slicehi
                figure;
                imshow(squeeze(img(:,n)), []);
                % title {[imgtitle,['Slicen',int2str(n)])};
                title([imgtitle, ':', 'Slicen', int2str(n)]);
            end
            return
        end

        for n = slicelo:slicehi

            % fourier method commented out
            f1img = fft2(squeeze(img(:,n)));
            f2img = fftshift(f1img);

            Fimg = f1img;
for i = 1:Nx
    for j = 1:Ny
        Fimg(i+Nxd, j+Nyd) = f2img(i, j);
    end
end
fintimg = ifft2(fftshift(Fimg), 'symmetric');

% figure
% imshow(fintimg, []);
% title(['imgtitle', 'slice', int2str(n)]);

% do the linear interpolation method
for i = 1:Nx-1
    for j = 1:Ny-1
        for k = 1:mag
            t = (k-1)/mag;
            for l = 1:mag
                u = (l-1)/mag;
                Lintimg(mag*(i-1)+k, mag*(j-1)+l) = ...
                (1-t)*(1-u)*img(i,j,n) + ...
                t*(1-u)*img(i+1,j,n) + ...
                (1-t)*u*img(i,j+1,n) + ...
                t*u*img(i+1,j+1,n);
                if i==1 && j==1
                    fprintf('%d %d : %f %f %f
', k, l, ...
                    (1-t)*(1-u), t*(1-u), (1-t)*u, t*u);
                end
            end
        end
    end
end

if colorflag == 0
    figure
    hold on
    imshow(Lintimg, []);
    title(['imgtitle', 'slice', int2str(n)]);
    colormap(gray);
    hold off
else
    figure
    hold on
    maxptile = prctile(imgvec(imgvec==0), 99);
    clims = [0 maxptile];
    imshow(Lintimg, clims);
    title(['imgtitle', 'slice', int2str(n)]);
    colormap(hot);
    colorbar;
    hold off
end
end

elseif strcmp(tes, 'ag')
    newimg = zeros(mag*[Ny Nz]);
    for n = slicelo:slicehi
        for i = 1:Ny
for j = 1:Nz
    for k = 1:mag
        for l = 1:mag
            newimg(mag*(i-1)+k, mag*(j-1)+l) = img(n,i,j);
        end
    end
end

figure
imshow(newimg, []);
title(imgtitle);
end

elseif strcmp(tcs,'cor')
newimg = zeros(mag*[Nx Nz]);

for n = slicelo:slicechi
    for i = 1:Nx
        for j = 1:Nz
            for k = 1:mag
                for l = 1:mag
                    newimg(mag*(i-1)+k, mag*(j-1)+l) = img(n,i,j);
                end
            end
        end
    end
end
figure
imshow(newimg, []);
title(imgtitle);
end
end
end
end

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init_moments.m

% allocate memory for new blob in blob array
% input-
% bimg: blob image array
% i: first pixel of new blob
% nblob: last blob number, will be incremented and returned
% fgflg: 1=foreground 0=background
% ny: number of columns
% output-
% nblob: new blob number
% blob1: new blob information
% adj_reg, and parents need to be set separately

function [nblob, blob1, bimg] = init_moments(i,nx,fgflg,parent,nblob,blob1,bimg)

    x = mod((i-1),nx)+1;
    y = floor((i-1)/nx)+1;
    z = 0;
nblob = nblob + 1;
bimg(i) = nblob;

blob1.fgfg = fgfg;
blob1.m000 = 1;
blob1.nblob = nblob;
blob1.parent = parent;
blob1.xbeg = x;
blob1.ybeg = y;
blob1.zbeg = z;
blob1.m100 = x;
blob1.m010 = y;
blob1.m001 = z;
blob1.m110 = x*y;
blob1.m101 = x*z;
blob1.m011 = y*z;
blob1.m200 = x^2;
blob1.m020 = y^2;
blob1.m002 = z^2;

return

10 pvroi.m

function pvroi(imgfile, slc, MDthresh)

close all

% Set assorted params
MDminarea = 20;
MDcendist = 20;
MDmax2mom = 200;

limnum = 4;
RAthresh = 0.18;
RAminarea = 25;
RAcendist = 25;

% read in file size from the ifh file
% form the file ifh file name
slen = max(size(imgfile));
ifhfile = [imgfile(1:(slen-3)) 'ifh'];
outfileFULL = [imgfile(1:(slen-3)) 'roiFULL'];
outfileCRNS = [imgfile(1:(slen-3)) 'roiCRNS'];
outfileRF = [imgfile(1:(slen-3)) 'roiRF'];
outfileL = [imgfile(1:(slen-3)) 'roiL'];
outfileRO = [imgfile(1:(slen-3)) 'roiRO'];
outfileLO = [imgfile(1:(slen-3)) 'roiLO'];
fprintf('Reading ifh file: %s
', ifhfile);

% read the ifh file
msize = zeros(1,4);
ndim = 1;
fid = fopen('thffile', 'r');
for j = 1:100
    tstr = fscanf(fid, '%s', 1);
    % fprintf('tstr = %s
', tstr);
    if strcmp(tstr, 'matrix')
        for i = 1:3
            tstr = fscanf(fid, '%s', 1);
        end
        msizem = fscanf(fid, '%d', 1);
    end
    ndim = ndim + 1;
end
if ndim == 5
    break
end
fclose(fid);

% check img dimensions from the thf file
fprintf('Input dimensions: %d %d %d %d %d
', msizem(1), msizem(2), msizem(3), msizem(4));

% basic error checking on slc
if msizem(3) < 3 || slc < 2 || slc > msizem(3) - 1
    fprintf('Error: invalid slice value or dimension.
');
    return
end

% image size in DTI space
N1 = msizem(1);
Ny = msizem(2);
Nz = msizem(3);
N1 = msizem(4);
N3D = N1*Ny*Nz;

% allocate memory for images
img1 = zeros([N1, Ny, Nz], 'single');
img2 = zeros([N1, Ny], 'single');
imgMD = zeros([N1, Nz], 'single');
imgRA = zeros([N1, Ny], 'single');
imgtmp = zeros([1 N3D], 'single');
imgtst = zeros([1 N3D], 'single');
imgoutFULL = zeros([N1, Ny, Nz], 'single');
imgoutCRNS = zeros([N1, Ny, Nz], 'single');
imgoutRF = zeros([N1, Ny, Nz], 'single');
imgoutLF = zeros([N1, Ny, Nz], 'single');
imgoutRO = zeros([N1, Ny, Nz], 'single');
imgoutLO = zeros([N1, Ny, Nz], 'single');

imgA = zeros([N1, Ny], 'single');
imgB = zeros([N1, Ny], 'single');
imgC = zeros([N1, Ny], 'single');
imgD = zeros([N1, Ny], 'single');

imga = zeros([N1, Ny], 'single');
imgb = zeros([N1, Ny], 'single');
imgc = zeros([N1, Ny], 'single');
imgd = zeros([N1, Ny], 'single');

imgm1 = zeros([N1, Ny], 'single');
imgm2 = zeros([N1, Ny], 'single');
imgm3 = zeros([Nx, Ny], 'single');
imgm4 = zeros([Nx, Ny], 'single');

imgr1 = zeros([Nx, Ny], 'single');
imgr2 = zeros([Nx, Ny], 'single');
imgr3 = zeros([Nx, Ny], 'single');
imgr4 = zeros([Nx, Ny], 'single');

%% Read input files
DTIdata = zeros([6, N3D], 'single');
fid = fopen(inputfile,'r');
for i = 1:1
    imgtmp = fread(fid, [1, N3D], 'float', '});
    DTIdata(:,i) = imgtmp(:,);
end

if i == 1
    imgtst = img3d(:,1,slc);
end

% display the slice(s) to focus on
imgDisp(img3d,'tra',slc,2,0,[inputfile(1:5)';DTT]);

% fclose(fid);

%% From here the program can do 1,2, or 3 slices saving the final ROIs
for ii = slc-1:slc+1

    % Display histogram of MD and RA
    img3d = reshape squeezes(DTIdata(:,i), [Nx, Ny, Nz]);
    imgMD = squeeze(img3d(:,ii));
    img3d = reshapesqueeze(DTIdata(:,i), [Nx, Ny, Nz]);
    imgRA = squeeze(img3d(:,ii));

    % histograms
    figure
    hist(reshape(imgMD,[1,numel(imgMD)]),100);
    ylim([0 1000]);
    title([inputfile(1:5)'; Distribution of MD on slice ' num2str(ii)]);

    MDmax = max(imgMD);)
    MDmin = min(imgMD);
    fprintf (MD min %f mode %f max %f\n',MDmin, MDmax);

    % simple threshold for MD and RA calculations
    imgA = (imgMD > MDthresh);
    imgA = (imgRA > RAthresh);

    % display after erode and dilate
    imgB = binerode(imgA, 5);
    imgC = bindilate(imgB, 5);
    imgD = zeros([Nx, Ny], 'single');
    imgB = binerode(imgA, 5);
    imgC = bindilate(imgB, 5);

    % MD analysis
    % find the blobs larger than 10 in size
    % nob1 is the total number of blobs, imgB only has the ones >= minarea
    % obival 1 nobj 2 mass 3 xcen 4 ycen 5 x2mom 6 y2mom

}
[nobj1, objval1, imgB] = find_blob(10, imgC);
% display blobs, 1 is coded as background
figure
imshow(imgB,[1 2]);

np = input('Input number of regions (default=1) then click on or near these regions: ');
if isempty(np) || np<=0
    fprintf('Error: number of regions must be >= 1\n');
    return
end

% IMPORTANT: different x,y convention in Matlab
[yx, xp] = ginput(np);
% save blobs close to clicks
for n = 1:np
    distmin = 100.0; k1 = 0;
    for k = 1:nobj1
        dist = sqrt((objval1(3,k) - xp(n))^2 + (objval1(4,k) - yp(n))^2);
        if dist < distmin
            distmin = dist;
            k1 = k;
        end
    end
end

% print the kept blobs
fprintf('MD nobj=%d area=%f distmin=%f\n',k1, objval1(2,k1), distmin);
for i = 2:Nx-1
    for j = 2:Ny-2
        if imgB(i,j)==objval1(1,k1)
            imgD(i,j) = 1;
        end
    end
end

% get perimeter
imgA = btrim(imgD, 2);
imgD = btrim(imgA, 2);
imgC = btrim(imgD, 2);
imgB = imgC - imgA;

% regions
close
figure
imshow(imgB,[]);
title([imgfile(1:5) '; Selected regions on slice ' num2str(ii)])

% RA analysis
RA_flag = 0; % use to suppress RA analysis
if RA_flag == 0
    [nobj2, objval2, imgb] = find_blob(25, imgc);
    figure
    imshow(imgb,[]);
end
% save blobs with area > minarea and near center
keepin = zeros(4,1);
index = 0;
img2d(Nx/2,Ny/2) = 2;
for k = 1:nobj2
decn = sqrt((objval2(3,k) - (Nx/2))^2 + (objval2(4,k) - (Ny/2))^2);
fprintf([''RA obj=%d area=%f decen=%f''],k,area,decn);

% keep if area above min and near center
if objval2(2,k) > Raminarea && decn < RAcendist
fprintf(''keep

index = index + 1;
if index >= 5
fprintf(''If index>5 need to fix program a bit: exiting now'');
return
end
keepin(index,1) = k;

% display all kept regions
for i = 2:Nx-1
for j = 2:Ny-2
if imgb(i,j)==objval2(1,k)
    img2d(i,j) = 1;
end
end
end
img2d(round(objval2(3,k)),round(objval2(4,k))) = 2;
end
end

figure
imshow(img2d,[]);

% select the best two
ymin = Ny; ymax = 0;
kmin = 0; kmax = 0;
for i = 1:index
if objval2(4,keepin(i,1)) < ymin
    ymin = objval2(4,keepin(i,1));
kmin = keepin(i,1);
end
if objval2(4,keepin(i,1)) > ymax
    ymax = objval2(4,keepin(i,1));
kmax = keepin(i,1);
end
end

% show kept blobs
% mark the kept blobs + shift them
for i = 2:Nx-1
for j = 2:Ny-2
if imgb(i,j)==objval2(1,kmin)
    imgd(i,j-2) = 1;
end
if imgb(i,j)==objval2(1,kmax)
    imgd(i,j+2) = 1;
end
end
end

figure
imshow(imgd,[]);
figure
imshow(imgtst,[ ]); 

figure
imshow(imgtst-imgtst.*imgd,[ ]); 

end

% store for output 
for m = 1:Nx 
    for n = 1:Ny 
        imgoutFULL(m,n,ii) = imgB(m,n); 
    end 
end 

imgoutCRNS(:,:,ii) = corners(imgB,limnum,Nx,Ny,5); 
imgoutRF(:,:,ii) = corners(imgB,limnum,Nx,Ny,1); 
imgoutLF(:,:,ii) = corners(imgB,limnum,Nx,Ny,2); 
imgoutRO(:,:,ii) = corners(imgB,limnum,Nx,Ny,3); 
imgoutLO(:,:,ii) = corners(imgB,limnum,Nx,Ny,4); 
end 

% slice loop on l 

% Store the output ROI 
fid = fopen(outfileFULL,'w'); 
fwrite(fid, imgoutFULL, 'float', 'T'); 
fclose(fid); 

fid = fopen(outfileCRNS,'w'); 
fwrite(fid, imgoutCRNS, 'float', 'T'); 
fclose(fid); 

fid = fopen(outfileRF,'w'); 
fwrite(fid, imgoutRF, 'float', 'T'); 
fclose(fid); 

fid = fopen(outfileLF,'w'); 
fwrite(fid, imgoutLF, 'float', 'T'); 
fclose(fid); 

fid = fopen(outfileRO,'w'); 
fwrite(fid, imgoutRO, 'float', 'T'); 
fclose(fid); 

fid = fopen(outfileLO,'w'); 
fwrite(fid, imgoutLO, 'float', 'T'); 
fclose(fid); 
tilefigs

return

samroi.m
Sample ROI on DTI data set
% inputs
function samroi(imgfile, slc)

close all

% read in file size from the ith file
% form the file ith file name
slen = max(size(imgfile));
ithfile = [imgfile(1:(slen-3)) 'itf';];
roiFILEFULL = [imgfile(1:(slen-3)) 'roiFULL';];
roiFILECRNS = [imgfile(1:(slen-3)) 'roiCRNS';];
roiFILERF = [imgfile(1:(slen-3)) 'roiRF';];
roiFILELF = [imgfile(1:(slen-3)) 'roiLF';];
roiFILERO = [imgfile(1:(slen-3)) 'roiRO';];
roiFILELO = [imgfile(1:(slen-3)) 'roiLO';];
fprintf('Reading ith file: %s
', ithfile);

msize = zeros(1,4);
ndim = 1;
fid = fopen(ithfile,'r');
for i = 1:100
tstr = fscanf(fid,'%s',1);
% fprintf('%d %s
',i,tstr);
if strcmp(tstr,'matrix')
    for i = 1:3
        tstr = fscanf(fid,'%s',1);
    end
    msize(ndim) = fscanf(fid,'%d',1);
    ndim = ndim + 1;
end
if ndim == 5
    break
end
end
fclose(fid);

% check img dimensions from the ith file
fprintf('Input dimensions: %d %d %d %d
',msize(1),msize(2),msize(3),msize(4));

% image size in DTI space
Nx = msize(1);
Ny = msize(2);
Nz = msize(3);
Nv = msize(4);
N3D = Nx*Ny*Nz;

% allocate memory for images
imgtmp = zeros([1, N3D], 'single');
imgroi = zeros([1, N3D], 'single');
imgsum = zeros([1, N3D], 'single');

% Read input files - Full trace
% read in roi file first
fid = fopen(roiFILEFULL,'r');
imgroi = fread(fid, [1, N3D], 'float', 't');
fclose(fid);

% number of fg pixels, assumes all=1
npix = sum(imgroi(:));
fprintf('Full trace npix = %d
',npix);

% read the different volume in loop and sample each
DTIdata = zeros([6, N3D], 'single');
 fid = fopen(imgfile,'r');
 for i = [1 9 12 13]
   imgtmp = fread(fid, [1, N3D], 'float', 'r');
   DTIdata(:,i,:) = imgtmp(:);
   imgsum = imgtmp.* imgroi;
   imgconf = imgtmp.* (1-imgroi);
   nsum = sum(imgsum(:));
   fprintf('%d
',nsum);
 end

%!!! displays for volumes of interest
if any(i == 1)
  % display heat maps for the 3 slices
  img3dinv = reshape(squeeze(imgconf1,:), [Nx, Ny, Nz]);
  ImgDisp(img3dinv, 'tra', slc-1, slc+1, 2, 1, [imgfile(1:5) ' corners; volume ' num2str(i)]);
end

fclose(fid);

% Read input files - Corners
% read in roi file first
 fid = fopen(roifileCRNS,'r');
 imgroi = fread(fid, [1, N3D], 'float', 'r');
 fclose(fid);

% number of fg pixels, assumes all=1
npix = sum(imgroi(:));
fprintf('Corners npix = %d
',npix);

% read the different volume in loop and sample each
DTIdata = zeros([6, N3D], 'single');
 fid = fopen(imgfile,'r');
 for i = [1 9 12 13]
   imgtmp = fread(fid, [1, N3D], 'float', 'r');
   DTIdata(:,i,:) = imgtmp(:);
   imgsum = imgtmp.* imgroi;
   imgconf = imgtmp.* (1-imgroi);
   nsum = sum(imgsum(:));
   fprintf('Corners ROI sampled on vol %d = %f
',i,nsum);
 end

%!!! displays for volumes of interest
if any(i == 1)
  img3dinv = reshape(squeeze(imgconf1,:), [Nx, Ny, Nz]);
  ImgDisp(img3dinv, 'tra', slc-1, slc+1, 2, 1, [imgfile(1:5) ' corners; volume ' num2str(i)]);
end
end
fclose(fid);

%% Read input files - RF
% read in roi file first
fid = fopen(roiFileRF,'r');
imgroi = fread(fid, [1, N3D], 'float', 't');
close(fid);

% number of fg pixels, assumes all=1
npix = sum(imgroi);
fprintf('RF npix = %d\n', npix);

% read the different volume in loop and sample each
DTIdata = zeros([6, N3D], 'single');
for i = [1 9 12 13]
    imgtmp = fread(fid, [1, N3D], 'float', 't');
    DTIdata(i,:) = imgtmp(:);
end

imgsum = imgtmp .* imgroi;
imgconf = imgtmp .* (1-imgroi);
nsnum = sum(imgsum(:));
fprintf('RF ROI sampled on vol %d = %d\n', i, nsnum*npix);

%!!! displays for volumes of interest
if any(i == 1)
    img3dinv = reshape(squeeze(imgconf(:, i)), [Nx, Ny, Nz]);
    ImgDisp(img3dinv, ['tra', slc-1, slc+1, 2, 1, [imgfile(1:5) ' RF; volume ' num2str(i)]);
end
end
fclose(fid);

%% Read input files - LF
% read in roi file first
fid = fopen(roiFileLF,'r');
imgroi = fread(fid, [1, N3D], 'float', 't');
close(fid);

% number of fg pixels, assumes all=1
npix = sum(imgroi);
fprintf('LF npix = %d\n', npix);

% read the different volume in loop and sample each
DTIdata = zeros([6, N3D], 'single');
for i = [1 9 12 13]
    imgtmp = fread(fid, [1, N3D], 'float', 't');
    DTIdata(i,:) = imgtmp(:);
end

imgsum = imgtmp .* imgroi;
imgconf = imgtmp .* (1-imgroi);
nsnum = sum(imgsum(:));
fprintf('LF ROI sampled on vol %d = %d\n', i, nsnum*npix);
%% displays for volumes of interest
if any(i == 1)

    img3dinv = reshape(squeeze(imgconf(1,:)), [Nx, Ny, Nz]);
    ImgDisp(img3dinv, 'tra', scl-1, scl+1, 2, 1, [imgfile(1:5) ' LF; volume ' num2str(i)]);

end

close(fid);

%% Read input files - RO
% read in roi file first
fid = fopen(roiFileRO,'r');
imgroi = fread(fid, [1, N3D], 'float', '');
close(fid);

% number of fg pixels, assumes all=1
npix = sum(imgroi(i,:));
fprintf('RO npix = %d \n',npix);

% read the different volume in loop and sample each
DTIdata = zeros([6, N3D], 'single');
for i = [1 9 12 13]
    imgtmp = fread(fid, [1, N3D], 'float', '');
    DTIdata(:,i) = imgtmp(:,);

    imgsum = imgtmp.*imgroi;
    imgconf = imgtmp.*(1-imgroi);
    nsum = sum(imgsum(:,));
    fprintf('RO ROI sampled on vol %d = %f \n',i,nsum/npix);

end
% displays for volumes of interest
if any(i == 1)

    img3dinv = reshape(squeeze(imgconf(1,:)), [Nx, Ny, Nz]);
    ImgDisp(img3dinv, 'tra', scl-1, scl+1, 2, 1, [imgfile(1:5) ' RO; volume ' num2str(i)]);

end

close(fid);

%% Read input files - LO
% read in roi file first
fid = fopen(roiFileLO,'r');
imgroi = fread(fid, [1, N3D], 'float', '');
close(fid);

% number of fg pixels, assumes all=1
npix = sum(imgroi(i,:));
fprintf('LO npix = %d \n',npix);

% read the different volume in loop and sample each
DTIdata = zeros([6, N3D], 'single');
for i = [1 9 12 13]

Data validation

The methods presented herein have been validated in a prospective cohort of human infants who were born preterm and sustained intraventricular hemorrhage with or without Posthemorrhagic hydrocephalus, in comparison to preterm infants with no identifiable brain injury and full term healthy infants [1]. To assess for potential differences between the algorithm and manually placed ROIs, dMRI of 20 neonates of varying ventricular morphologies were selected and manual ROIs were placed by an expert rater. Pearson correlation analyses between dMRI measures from both approaches indicated there was a strong positive association between the automated and manual segmentations fractional anisotropy \((r(20) = .91, p < .001)\) and MD \((r(20) = .89, p < .001)\) measures.

Conclusion

We describe a novel semi-automated segmentation algorithm that is able to generate ROIs isolating the perimeter of the lateral ventricles in diffusion-based brain MRI. The algorithm has robust fidelity for locating periventricular regions compared to manually produced ROIs and performs well in various situations of high-grade brain injury and ventriculomegaly. An additional step enables isolation of frontal and occipital regions of the periventricular ROI for separate analysis. Importantly, this method is able to extract regions associated with the ventricular system from other CSF spaces (cysts, cisterns, subarachnoid spaces), which has not been previously possible using traditional approaches.

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Declaration of Competing Interest

Dr. Limbrick receives research funds and/or research equipment for unrelated projects from Medtronic, Inc., Karl Storz, Inc., and Microbot Medical, Inc. Dr. Limbrick has received philanthropic equipment contributions for humanitarian relief work from Karl Storz, Inc. and Aesculap, Inc. The authors have no personal, financial, or institutional interest in any of the materials, or devices described in this article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.mex.2020.101023.

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