Appendix 1

As described in the Methods section, we can model a lymph node as an ellipsoid centred at the Cartesian origin with long axis 2c, intermediate axis 2b and short axis 2a:

(1)
$$\frac{x^2}{a^2}+\frac{y^2}{b^2}+\frac{z^2}{c^2}=1,$$
$$0<a\leq b<c$$

When slicing the lymph node parallel to the short axis at position $z = z_0$, $-c < z_0 < c$, we have the following ellipse as the trace:

(2)
$$\frac{x^2}{a^2}+\frac{y^2}{b^2}=1-\frac{z_0^2}{c^2}$$

This ellipse has the standard form:

(3)
$$\frac{x^2}{\left(a\sqrt{1-\frac{z_0^2}{c^2}}\right)^2}+\frac{y^2}{\left(b\sqrt{1-\frac{z_0^2}{c^2}}\right)^2}=1$$

which, accordingly, has semi-axes:

$$a\sqrt{1-\frac{z_0^2}{c^2}},b\sqrt{1-\frac{z_0^2}{c^2}}$$

Or, when generalized for *z* as an independent variable such that $-c < z < c$, (4, 5) $$a\sqrt{1-\frac{z^2}{c^2}},b\sqrt{1-\frac{z^2}{c^2}}$$

We can then compute the area of individual ellipses for a given *z* by the equation:

(6) $$A_{\text{Parallel to short axis}}(z)=\pi\left(\left(a\sqrt{1-\frac{z^2}{c^2}}\right)\left(b\sqrt{1-\frac{z^2}{c^2}}\right)\right)$$
$$=\pi ab\left(1-\frac{z^2}{c^2}\right)$$

By the same logic, we can obtain the area of the individual ellipses taken through slices parallel to the long axis (assuming, without loss of generality, that it is the x-axis) as per:

(7) $$A_{\text{Parallel to long axis}}(x)=\pi bc\left(1-\frac{x^2}{a^2}\right)$$

Looking more carefully at equations (6) and (7), we can see that the smaller the values of *z* or *x* that are input, the greater the individual ellipse cut surface areas; this explains why we should make our first cut at the centre of the node upon grossing (where both *z* and *x* will be equal to 0), followed by further cuts moving outwards from the centre, regardless of the specific approach. Now, assume that we take sections every 2 mm and (again with axes lengths as above), and that we begin by slicing centrally and move outward. Furthermore, assume that for each slice, the greater of the two cut surface areas is exposed when embedding. Under these assumptions, the sum total cut surface area on sectioning when slicing parallel to the short axis can be given by:

(8)
$$2\sum_{n=0}^{\left\lfloor \frac{c}{2} \right\rfloor} A_{\text{Parallel to short axis}}(2n)$$

where $\lfloor x \rfloor$ is the floor function which returns the integer n such that, for $x \in \Re$, $n \le x < n+1$ (i.e. the next lowest integer)

This can be simplified as per:

(9)
$$2\sum_{n=0}^{\left\lfloor \frac{c}{2} \right\rfloor} A_{\text{Parallel to short axis}}(2n) = 2\pi ab\left(\sum_{n=0}^{\left\lfloor \frac{c}{2} \right\rfloor} 1 - \tfrac{4}{c^2}\sum_{n=0}^{\left\lfloor \frac{c}{2} \right\rfloor} n^2\right)$$
$$= 2\pi ab\left(\left\lfloor \frac{c}{2} \right\rfloor + 1 - \tfrac{4}{6c^2}\left(\left\lfloor \frac{c}{2} \right\rfloor\left(\left\lfloor \frac{c}{2} \right\rfloor + 1\right)\left(2\left\lfloor \frac{c}{2} \right\rfloor + 1\right)\right)\right)$$

Similarly, the long axis approach is given by:

(10)
$$2\sum_{m=0}^{\left\lfloor \frac{a}{2} \right\rfloor} A_{\text{Parallel to long axis}}(2m) = 2\pi bc\left(\sum_{m=0}^{\left\lfloor \frac{a}{2} \right\rfloor} 1 - \tfrac{4}{a^2}\sum_{m=0}^{\left\lfloor \frac{a}{2} \right\rfloor} m^2\right)$$
$$= 2\pi bc\left(\left\lfloor \frac{a}{2} \right\rfloor + 1 - \tfrac{4}{6a^2}\left(\left\lfloor \frac{a}{2} \right\rfloor\left(\left\lfloor \frac{a}{2} \right\rfloor + 1\right)\left(2\left\lfloor \frac{a}{2} \right\rfloor + 1\right)\right)\right)$$

Thus using (9) and (10), we can calculate the ideal exposed cut surface area for each of the long and short axes approaches, respectively.

Appendix 2

The following code was used to compute the lymph node length matrix (Figure 3) using MATLAB:

```
%the cell X(i,j) = -1, 0, 1 denotes that the lymph node with long and short axes i and j (depending
%on which of i or j is greater) as having best grossing with the shot axis, with either or with the
%long axis protocols, respectively
X = zeros(40);
a=0; c=0;
for l=1:40
    for s=1:40
        if(l>s)
            a=s; c=l; a=0.5*a; c=0.5*c;
            if (a*(floor(c/2)+1-(4/(6*(c^2)))*(floor(c/2)*(floor(c/2)+1)*(2*floor(c/2)+1)))>c*(floor(a/2)+1-
(4/(6*(a^2)))*(floor(a/2)*(floor(a/2)+1)*(2*floor(a/2)+1))))
                X(s,l)=-1;
            elseif (a*(floor(c/2)+1-
(4/(6*(c^2)))*(floor(c/2)*(floor(c/2)+1)*(2*floor(c/2)+1)))<c*(floor(a/2)+1-
(4/(6*(a^2)))*(floor(a/2)*(floor(a/2)+1)*(2*floor(a/2)+1))))
                X(s,l)=1;
             else
                X(s,l)=0;
            end
        else
            a=l; c=s; a=0.5*a; c=0.5*c;
            if (a*(floor(c/2)+1-(4/(6*(c^2)))*(floor(c/2)*(floor(c/2)+1)*(2*floor(c/2)+1)))>c*(floor(a/2)+1-
(4/(6*(a^2)))*(floor(a/2)*(floor(a/2)+1)*(2*floor(a/2)+1))))
                X(s,l)=-1;
```

```
            elseif (a*(floor(c/2)+1-
(4/(6*(c^2)))*(floor(c/2)*(floor(c/2)+1)*(2*floor(c/2)+1)))<c*(floor(a/2)+1-
(4/(6*(a^2)))*(floor(a/2)*(floor(a/2)+1)*(2*floor(a/2)+1))))
                X(s,l)=1;
            else
                X(s,l)=0;
            end
        end
    end
end
```

Appendix 3

```
%program for comparing the "optimal" and “non-optimal” grossing approaches on randomly
%sized/located foci of metastasis (smaller than a microfocus)
processArray=zeros(1000, 3);
for r=1:1:1000
stopCounter=0;
goodCount=0;
badCount=0;
bothCount=0;
while(stopCounter <= 1000)
   n=40;
   f=ceil(n.*rand(3,1));
   AxesArray = sort(f);
%axis lengths as random integers between 1 and 40 inclusive
   a = AxesArray(1);
   b = AxesArray(2);
   c = AxesArray(3);
%random position values between -20 and 20
   x = -20*rand + 20*rand;
   y = -20*rand + 20*rand;
   z = -20*rand + 20*rand;
   if ( (x/(0.5*a))^2 + (y/(0.5*b))^2 + (z/(0.5*c))^2 < 1)
%to ensure that the focus is contained within the node itself
```

```
    ITC = 0.2*rand;
%to ensure that the focus of ITCs is less than a microfocus
    if (X(a, c) == -1)
      oldGoodCount = goodCount;
      oldBadCount = badCount;
      for k=0:2:floor(c/2)
        if ( (z-ITC<k && z+ITC>k) || (z-ITC<-k && z+ITC>-k))
          goodCount=goodCount+1;
        end
      end
      for k=0:2:floor(a/2)
        if ( (x-ITC<k && x+ITC>k) || (x-ITC<-k && x+ITC>-k))
          badCount=badCount+1;
        end
      end
      if(goodCount-oldGoodCount>0 && badCount-oldBadCount>0)
        bothCount=bothCount+1;
      end
      stopCounter=stopCounter+1;
    elseif (X(a, c) == 1)
      oldGoodCount = goodCount;
      oldBadCount=badCount;
      for k=0:2:floor(a/2)
```

```
            if ( (x-ITC<k && x+ITC>k) || (x-ITC<-k && x+ITC>-k) )
                goodCount=goodCount+1;
            end
        end
        for k=0:2:floor(c/2)
            if ( (z-ITC<k && z+ITC>k) || (z-ITC<-k && z+ITC>-k) )
                badCount=badCount+1;
            end
        end
        if(goodCount-oldGoodCount>0 && badCount-oldBadCount>0)
            bothCount=bothCount+1;
        end
        stopCounter=stopCounter+1;
    else
%exclude spherical lymph nodes
    end
  end
end
processArray(r, 1) = goodCount;
processArray(r, 2) = badCount;
processArray(r, 3) = bothCount;
end
```