Part 1:
4.1 
a. The estimate of the survival function at 1 year (12 months) is 0.90385 with a standard error of 0.040882. The estimate of the survival function at 5 years (60 months) is 0.65385 with a standard error of 0.065974. (See page 11)
b. The cumulative hazard rate at 60 months is 0.41780 with standard error of 0.09921. The estimate of $S(60)$ obtained by exp{-0.41780} is 0.65849. This estimate is slightly higher than the estimate we found in part a. (See page 11)
c. The 95% linear confidence interval for $S(60)$ is (0.52454, 0.78315). (See page 11)
f&g. The confidence bands for the cumulative hazard rate using both the EP and Hall-Wellner methods were found using the appropriate confidence coefficients of c(.3, .42) (calculated from equation 4.4.8 in the book). The range of 3 to 6 years was adjusted for actual time points to 32-72 months. The results were as follows (See page 11): 

<table>
<thead>
<tr>
<th>t2</th>
<th>epL</th>
<th>epU</th>
<th>hwL</th>
<th>hwU</th>
</tr>
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<tbody>
<tr>
<td>32</td>
<td>0.50375</td>
<td>0.82102</td>
<td>0.49934</td>
<td>0.82307</td>
</tr>
<tr>
<td>41</td>
<td>0.48433</td>
<td>0.80559</td>
<td>0.48358</td>
<td>0.80596</td>
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<tr>
<td>51</td>
<td>0.46516</td>
<td>0.78989</td>
<td>0.46747</td>
<td>0.78868</td>
</tr>
<tr>
<td>65</td>
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<td>0.77359</td>
<td>0.45040</td>
<td>0.77082</td>
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<tr>
<td>67</td>
<td>0.42596</td>
<td>0.75702</td>
<td>0.43310</td>
<td>0.75284</td>
</tr>
<tr>
<td>70</td>
<td>0.40679</td>
<td>0.74019</td>
<td>0.41562</td>
<td>0.73476</td>
</tr>
<tr>
<td>72</td>
<td>0.38789</td>
<td>0.72311</td>
<td>0.39800</td>
<td>0.71659</td>
</tr>
</tbody>
</table>

h. An estimate of the mean survival time restricted to 400 months is 146.645. This restricted mean survival time had a 95% confidence interval of (92.1404, 201.150). (See page 12)
i. An estimate of the median time to death was 93. Based on a linear confidence interval, the 95% confidence interval for the median survival time is (67,157). (See page 11)

7.4 
a. Using the log-rank test, we do not reject the null hypothesis that the survival rates of patients with cancer of the tongue are the same for patients with aneuploid and diploid tumors since the log-rank test showed a P-value of 0.0949. (See page 12)
b. If the primary interest is in detecting differences in survival rates between the two types of cancers which occur soon after the diagnosis of the cancer, a more appropriate test statistic would be Gehan’s test statistic because it weights earlier comparisons heavier. The Gehan’s test statistic is also referred to as the Wilcoxon test statistic when the STRATA command is used under the LIFETEST procedure (according to support.sas.com/documentation). According to the Wilcoxon/Gehan’s test, we do not reject the null hypothesis since the test resulted in a P-value of 0.0690. (See page 12)

8.3 
a. When we use the Breslow method to handle ties, the score test of the hypothesis of no effect of ploidy on survival gives us a P-value of 0.0975. (See page 12)
b. Using the Breslow method of handling ties, the estimate of $\beta$ is -0.46104 with a standard error of 0.28053. The relative risk is 0.631. The 95% confidence interval for the relative risk of
death of an individual with an aneuploid tumor as compared to an individual with a diploid tumor is (0.364, 1.093). (See page 12) 
c. When we use the Breslow method to handle ties, the likelihood test gives us a P-value of 0.1061. This P-value is slightly larger than the P-value found in part A, however both neither are significant, therefore in both cases we reject the null hypothesis (stated in part A). (See page 12) 
d. When we use the Breslow method to handle ties, the Wald test gives us a P-value of 0.1003. This P-value is slightly larger than the P-value found in part A and slightly smaller than the P-value we found in part C. None of these P-values are significant, therefore in all cases we reject the null hypothesis (stated in part A). (See page 12) 

5. 
a. The plot of the logarithms of the cumulative baseline hazard rates can be found on page 13. This plot is suggestive of nonproportional hazards. 
b. The plot of the difference in the log cumulative hazard rates can be found on page 13. This plot is suggestive of nonproportional hazards. 
c. An Anderson plot can be found on page 14. This plot is suggestive of nonproportional hazards. 

But the bad, close to proportional except at early stage and late. 

6. 
a. The plot of the Cox-Snell residuals can be found on page 14. The model seems to fit the data fairly well. 
b. The plot of the Martingale residuals can be found on page 15. There are a few outliers in both types of tumors (highlighted) 
c. The plot of the deviance residuals can be found on page 15. 
d. When we fit the data to the Weibull model in homework 3 to test the hypothesis of no effect of ploidy, we found that the Wald test and the Likelihood Ratio test both gave the same P-value, namely P= 0.057. When we fit the data to the log logistic model in homework 3 to test the hypothesis of no effect of ploidy, we found that the Wald test and the Log Likelihood Ratio test also both gave the same P-value, namely P= 0.051. Therefore, we cannot reject the null hypothesis that there is no effect of ploidy for either model (using 0.05 for alpha). The semi-parametric models showed slightly less of an effect of ploidy on survival for patients, with the score test, the likelihood test, and the Wald test resulting in P-values of 0.0975, 0.1061, and 0.1003 respectively. We cannot reject the null hypothesis for any of the semi-parametric tests. In terms of nonparametric models, we saw that log-rank test resulted in a P-value of 0.0949 and Wilcoxon/Gehan’s resulted a P-value of 0.0690. Again, we cannot reject the null hypothesis. In general, the parametric models are closest to approaching significance, followed by the nonparametric models, then finally followed by the semi-parametric models. Overall, none of the models conclusively show evidence to reject the null hypothesis. 

But which model fits data better?
Part 2:
4.1
data tongue;
input g t2 dfree;
cards;
  1  1  1
  1  3  1
  1  3  1
  1  4  1
  1 10 1
  1 13 1
  1 13 1
  1 16 1
  1 16 1
  1 24 1
  1 26 1
  1 27 1
  1 28 1
  1 30 1
  1 30 1
  1 32 1
  1 41 1
  1 51 1
  1 65 1
  1 67 1
  1 70 1
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  1 77 1
  1 91 1
  1 93 1
  1 96 1
  1 100 1
  1 104 1
  1 157 1
  1 167 1
  1 61 0
  1 74 0
  1 79 0
  1 80 0
  1 81 0
  1 87 0
  1 87 0
  1 88 0
  1 89 0
  1 93 0
  1 97 0
  1 101 0
  1 104 0
  1 108 0
  1 109 0
  1 120 0
  1 131 0
  1 150 0
  1 231 0
  1 240 0
1 400 0
2 1 1
2 3 1
2 4 1
2 5 1
2 5 1
2 8 1
2 12 1
2 13 1
2 18 1
2 23 1
2 26 1
2 27 1
2 30 1
2 42 1
2 56 1
2 62 1
2 69 1
2 104 1
2 104 1
2 112 1
2 129 1
2 181 1
2 8 0
2 67 0
2 76 0
2 104 0
2 176 0
2 231 0

; proc sql;
create table raw_dataAneuploid as
  select t2, sum(dfree) as num_event, count(t2) as sub_total
  from tongue
  where g = 1
  group by t2;
quit;

data tableAneuploid;
set raw_dataAneuploid nob = all;
total1 = lag(sub_total);
retain num_left 52;
if _n_ > 1 then do;
  num_left = - total1 + num_left; end;
retain surv 1 delta h sigma2 0;
surv = surv*(1-num_event/num_left);
delta= delta + num_event/(num_left*(num_left-num_left));
var = (surv**2)*delta;
stderr = var**.5;
h = h + num_event / num_left;
sigma2 = sigma2 + num_event /(num_left)**2;
stderrh = sigma2**.5;
if num_event==0 or _n_ = all;
run;

data tableAneuploid_c;
set tableAneuploid;
if surv ~= . then sigma = stderr / surv;
md = probit(1-.05/2)*sigma ;
linearL = surv - md * surv;
linearU = surv + md * surv;
run;

proc print data = tableAneuploid noobs;
Title 'Table Aneuploid';
var t2 num_event num_left surv stderr h stderrh;
run;

proc lifetest data = tongue;
time t2*dfree(0);
where g = 1;
survival out=part_i confotype=linear;
run;

Proc print data = tableAneuploid_c noobs;
Title 'Table Aneuploid 95% CI';
var t2 surv var stderr sigma;
var linearL linearU;
where t2 = 51;
run;

data tableAneuploid_fg;
set tableAneuploid;
if surv ~= . then sigma = stderr / surv;
md = probit(1-.05/2)* sigma ;
md1 = 2.4783*sigma ;
md2 = 1.1796*(1+52*sigma2)/52**.5;
epL = surv**( 1 / (exp( md1 /log(surv))));
epU = surv**(exp( md1 /log(surv)));
hwL = surv**( 1 / (exp( md2 /log(surv))));
hwU = surv**(exp( md2 /log(surv)));
if 32 <=t2 <=72 ;
run;

proc print data=tableAneuploid_fg noobs;
Title 'Table Aneuploid 95% EP and HW';
var t2 surv stderr sigma2 epL epU hwL hwU;
run;

proc sort data= tableAneuploid;
by descending t2;
run;
proc sql;
select min(t2) into :mint
from tableAneuploid;
quit;
data tableAneuploid_h;
set tableAneuploid nobs = last;
lagt = lag(t2);
if _n_ = 1 then
med = surv*(400 - t2);
else med = surv*(lagt- t2); output;
if _n_ =last then do; med = &mint; output; end;
run;

data tableAneuploid_h1;
set tableAneuploid_h nobs=last;
retain sumd vmean 0;
sumd = sumd + med;
vmean = vmean + ( sumd**2 ) * num_event/(num_left*(num_left-num_event));
if _n_ =last then vmean=sqrt(vmean);
run;

data tableAneuploid_h2;
set tableAneuploid_h1 nobs=last;
if _n_ =last then do;
stderr = vmean;
clow = sumd - 1.96*stderr;
chigh = sumd + 1.96*stderr;
end;
if _n_ ^= last then delete;
run;

proc print data = tableAneuploid_h2 noobs ;
Title 'Aneuploid Mean time to Death with CI';
var sumd stderr clow chigh;
run;

7.4
data tongue;
proc lifetest;
strata g;
time t2*dfree(0);
run;

8.3
data tongue1;
set tongue;
if g = 1 then zl=1;
if g = 2 then zl=0;
run;
proc phreg data=tongue1 ;
model t2*dfree(0)= zl /itprint risklimits;
run;

5.
data tongue_a;
set tongue;
cons = 1;
g1 = g - 1;
run;

proc phreg data = tongue_a ;
model t2*dfree(0) = cons;
strata g1;
output out = figure11_6 logsurv = ls /method = ch;
run;
data figure11_6a;
set figure11_6;
logh = log (-ls);
if g1 = 0 then logh1 = logh;
if g1 = 1 then logh2 = logh;
run;

proc sort data = figure11_6a;
by t2;
run;

options label;
goptions reset = all;
title "Plot of log cumulative baseline hazard rates versus time on study";
axis1 order = (0 to 400 by 50) minor = none;
axis2 order = (-4 to 1 by 1) minor = none label = ( a=90);
symbol1 i = stepjl c= blue;
symbol2 i = stepjl c = red l = 3;

legend label=none value=('Aneuploid' 'Diploid')
position=(bottom right inside) mode=share cborder=black;

proc gplot data = figure11_6a;
plot logh1*t2 = 1 logh2*t2 = 2 /overlay haxis=axis1 vaxis=axis2 legend = legend1;
label logh1 = "Log Cumulative Hazard Rate";
label t2 = "Time on Study";
run;
quit;

data figure11_6b;
set figure11_6a;
retain 11 12 13;
if logh1 ~= . then 11 = logh1;
if logh2 ~= . then 12 = logh2;
diff = 12 - 11;
r
run;
goptions reset = all;
axis1 order = (0 to 400 by 50) minor = none;
axis2 order = (-1.5 to 1 by .5) minor = none label = ( a=90);
symbol1 i = stepjl c= blue;
title "Difference in log cumulative baseline hazard rates (Diploid-Aneuploid) versus time on study";
proc gplot data = figure11_6b;
plot diff*t2 /haxis= axis1 vaxis=axis2 vref=0;
label diff = "Difference in Cumulative Hazard Rates";
label t2 = "Time on Study";
run;
quit;

data figure11_6c;
set figure11_6b;
retain h1 h2 0;
if g1 = 0 then h1 = -ls;
if g1 = 1 then h2 = -ls;
run;

proc sort data = figure11_6c;
   by ll;
run;

symbol1 c = blue i = stepjl;
symbol2 c = black i = join;
title "Andersen Plot";
axis1 order = (0 to 1 by .2) minor = none;
axis2 order = (0 to 1 by .2) minor = none label = ( a=90);

proc gplot data = figure11_6c;
   plot h2*h1 = 1 h1*h1=2 /overlay haxis = axis1 vaxis = axis2;
   label h2 = "Diploid";
   label h1 = "Aneuploid";
run;
quit;

6.
data tongue1;
set tongue;
if g = 1 then z1=1;
if g = 2 then z1=0;
run;

proc phreg data = tongue1;
model t2*dfree(0) = z1;
output out = figure11_1 LOGSURV = h;
run;

data figure11_1a;
set figure11_1;
   h = -h;
   cons = 1;
run;

proc phreg data = figure11_1a ;
model h*dfree(0) = cons;
output out = figure11_1b logsurv = 1s /method = ch;
run;

data figure11_1c;
set figure11_1b;
haz = - 1s;
run;

proc sort data = figure11_1c;
by h;
run;

goptions reset=all;
title "Cox-Snell residual plot";
axis1 order = (0 to 2.5 by .5) minor = none;
axis2 order = (0 to 2.5 by .5) minor = none label = ( a=90);
symbol1 i = stepj1 c= blue;
symbol2 i = join c = red l = 3;

proc gplot data = figure11_1c;
plot haz*h =1 h*h =2 /overlay haxis=axis1 vaxis= axis2;
label haz = "Estimated Cumulative Hazard Rates";
label h = "Residual";
run;
quit;

proc sort data = figure11_1a;
   by z1;
run;
proc phreg data = figure11_1a;
   model h*dfree(0) = cons;
   output out = fill_2b logsurv = 1s /method = ch;
      by z1;
run;
data fill_2b1;
   set fill_2b;
      if z1 = 0 then haz1 = -1s;
      if z1 = 1 then haz2 = -1s;
run;
proc sort data = fill_2b1;
   by h;
run;

title "Cox-Snell Residuals";
symbol1 i = stepj1 c= blue;
symbol2 i = stepj1 c = red l = 3;
symbol3 i = join c = black;

legend label=none value=("Aneuploid" 'Diploid' '45 degree line')
   position=(bottom right inside) mode=share cborder=black;

proc gplot data = fill_2b1;
   plot haz1*h = 1 haz2*h = 2 h*h=3 /overlay haxis=axis1 vaxis=axis2 legend =
      legend1;
   label haz1 = "Log Cumulative Hazard Rate";
   label h = "Residual";
run;
quit;

PROC PHREG DATA=tongue;
MODEL t2*dfree(0) = g;
OUTPUT OUT=outp XBETA=xb RESMART=mart RESDEV=dev RESCH =ressch LMAX=lmax 
   RESSCO=ressco; RUN;

PROC GLOT DATA=outp ;
TITLE1 "Martingale residuals plot";
PLOT mart*xb /CFRAME=white OVERLAY VAXIS=axis1 HAXIS=axis2 FRAME VREF=0 
   VMINOR=0 HMINOR=0 
   CAXIS = BLACK NAME="plot3";
symbol1 i= none v= dot c= blue;
AXIS1 LABEL=(A=90 R=0 F="<tt>Arial" "Martingale Residual")WIDTH=2;
AXIS2 LABEL=("Linear Predictor") VALUE=none WIDTH=2; RUN; QUIT;
DATA INF;
SET outp(where =(dev ne .));
id_t2;
LENGTH text $12 function $8;
RETAIN XSYS 'Z' YSYS 'Z' size 1;
X=xb ; Y=dev;
IF abs(dev) > 2.5 THEN DO; function= 'LABEL'; position= '8'; TEXT=ID; END;
RUN;

GOPTIONS RESET=all COLORS=(Black, RED, BLUE, YELLOW, GREEN, MAGENTA, CYAN) dev=EMF
target=EMF
XMAX=7 YMAX=7 HTEXT=14pt FTEXT="<tt> Arial";

PROC GPLOT DATA=outp ;
TITLE1 "Deviance residuals plot";
TITLE2 "Outlier and influential diagnostics ";
BUBBLE dev*xb=lmax /CFRAME=white ANNOTATE=inf VAXIS=axis1 HAXIS=axis2 FRAME
VREF=-2.5 0 2.5
VMINOR=0 HMINOR=0 CAXIS= black NAME='plot3' BCOLOR=red BSIZE=12;
AXIS1 LABEL=(A=90 R=0 F="Arial " "Deviance Residual")WIDTH=2; RUN;
QUIT;
### Part 3:

#### 4.1

<table>
<thead>
<tr>
<th>t2</th>
<th>event</th>
<th>num_left</th>
<th>surv</th>
<th>stderr</th>
<th>h</th>
<th>stderrh</th>
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<tr>
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<td>0.22886</td>
<td>0.095405</td>
<td>1.39131</td>
<td>0.37518</td>
</tr>
<tr>
<td>400</td>
<td>0</td>
<td>1</td>
<td>0.22886</td>
<td>0.095405</td>
<td>1.39131</td>
<td>0.37518</td>
</tr>
</tbody>
</table>

**Quartile Estimates**

<table>
<thead>
<tr>
<th>Percent</th>
<th>Estimate</th>
<th>Transform</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>75</td>
<td>167.00</td>
<td>LINEAR</td>
<td>104.000</td>
</tr>
<tr>
<td>50</td>
<td>93.00</td>
<td>LINEAR</td>
<td>67.000  157.000</td>
</tr>
<tr>
<td>25</td>
<td>29.00</td>
<td>LINEAR</td>
<td>16.000  67.000</td>
</tr>
</tbody>
</table>

**Table Aneploid 95% CI**

<table>
<thead>
<tr>
<th>t2</th>
<th>surv</th>
<th>var</th>
<th>stderr</th>
<th>sigmas</th>
<th>linearL</th>
<th>linearU</th>
</tr>
</thead>
<tbody>
<tr>
<td>51</td>
<td>0.65385</td>
<td>0.00435226</td>
<td>0.065974</td>
<td>0.109090</td>
<td>0.52454</td>
<td>0.78315</td>
</tr>
</tbody>
</table>

**Table Aneploid 95% EP and HW**

<table>
<thead>
<tr>
<th>t2</th>
<th>surv</th>
<th>stderr</th>
<th>sigmas</th>
<th>epL</th>
<th>epU</th>
<th>hwL</th>
<th>hwU</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>0.69231</td>
<td>0.064004</td>
<td>0.038255</td>
<td>0.50375</td>
<td>0.82102</td>
<td>0.49934</td>
<td>0.82307</td>
</tr>
<tr>
<td>41</td>
<td>0.67308</td>
<td>0.065051</td>
<td>0.039027</td>
<td>0.48433</td>
<td>0.80559</td>
<td>0.48358</td>
<td>0.80596</td>
</tr>
<tr>
<td>51</td>
<td>0.65385</td>
<td>0.065974</td>
<td>0.039843</td>
<td>0.46516</td>
<td>0.78989</td>
<td>0.46747</td>
<td>0.78868</td>
</tr>
<tr>
<td>65</td>
<td>0.63403</td>
<td>0.066884</td>
<td>0.040762</td>
<td>0.44541</td>
<td>0.77359</td>
<td>0.45040</td>
<td>0.77062</td>
</tr>
<tr>
<td>67</td>
<td>0.61422</td>
<td>0.067665</td>
<td>0.041738</td>
<td>0.42596</td>
<td>0.75702</td>
<td>0.43310</td>
<td>0.75284</td>
</tr>
<tr>
<td>70</td>
<td>0.59441</td>
<td>0.068321</td>
<td>0.042779</td>
<td>0.40679</td>
<td>0.74019</td>
<td>0.41362</td>
<td>0.73476</td>
</tr>
<tr>
<td>72</td>
<td>0.57459</td>
<td>0.068857</td>
<td>0.043800</td>
<td>0.38799</td>
<td>0.72311</td>
<td>0.39800</td>
<td>0.71659</td>
</tr>
</tbody>
</table>
Aneuploid Mean time to Death with CI

<table>
<thead>
<tr>
<th>round</th>
<th>stderr</th>
<th>clow</th>
<th>chigh</th>
</tr>
</thead>
<tbody>
<tr>
<td>146.645</td>
<td>27.8085</td>
<td>92.1404</td>
<td>201.150</td>
</tr>
</tbody>
</table>

### 7.4

Test of Equality over Strata

<table>
<thead>
<tr>
<th>Test</th>
<th>Chi-Square</th>
<th>DF</th>
<th>Pr &gt; Chi-Square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log-Rank</td>
<td>2.7897</td>
<td>1</td>
<td>0.0949</td>
</tr>
<tr>
<td>Wilcoxon</td>
<td>3.3055</td>
<td>1</td>
<td>0.0690</td>
</tr>
<tr>
<td>-2Log(LR)</td>
<td>3.9481</td>
<td>1</td>
<td>0.0469</td>
</tr>
</tbody>
</table>

### 8.3

The PHREG Procedure

Testing Global Null Hypothesis: BETA=0

<table>
<thead>
<tr>
<th>Test</th>
<th>Chi-Square</th>
<th>DF</th>
<th>Pr &gt; ChiSq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likelihood Ratio</td>
<td>2.6115</td>
<td>1</td>
<td>0.1061</td>
</tr>
<tr>
<td>Score</td>
<td>2.7464</td>
<td>1</td>
<td>0.0975</td>
</tr>
<tr>
<td>Wald</td>
<td>2.7009</td>
<td>1</td>
<td>0.1003</td>
</tr>
</tbody>
</table>

Analysis of Maximum Likelihood Estimates

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DF</th>
<th>Parameter Estimate</th>
<th>Standard Error</th>
<th>Chi-SquareP</th>
<th>Pr &gt; ChiSq</th>
</tr>
</thead>
<tbody>
<tr>
<td>z1</td>
<td>1</td>
<td>-0.46104</td>
<td>0.28053</td>
<td>2.7009</td>
<td>0.1003</td>
</tr>
</tbody>
</table>

Analysis of Maximum Likelihood Estimates

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Hazard Ratio</th>
<th>95% Hazard Ratio Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>z1</td>
<td>0.631</td>
<td>0.364</td>
</tr>
</tbody>
</table>
5. 

Plot of log cumulative baseline hazard rates versus time on study

Difference in log cumulative baseline hazard rates (Diploid-Aneuploid) versus time on study

This is artificial, start from time = 1.
Andersen Plot

Cox-Snell Residuals
Martingale residuals plot

Deviance residuals plot
Outlier and influential diagnostics

This martingale residual plot may not be symmetric as explained in the textbook.