cells. Then only three more doubling times would be
required, from 1% to 2%, to 4%, and to 8%, in order
to bring the shell up to the previous example, for a total
of eight doubling times for the tumor to recur larger
than its original volume.

These calculations assume that the infiltrating cells
can be recognized microscopically because they are as
pleomorphic as those in the main mass of the tumor excised,
but this is rarely the case since most gliomas tend to
become less pleomorphic beyond the grossly
obvious edge,1 leading inevitably to difficulty in defining
exactly where the edge really is and just what
percentage contamination there is in the shell remaining
after excision. Needless to say, if the infiltrating glioma
extends several centimeters beyond the gross edge,4 the
volume of tumor remaining in the shell greatly exceeds
the amount excised, as can be visualized by an extension
of Fig. 2.

From the above estimates, is it any wonder that even
radical excisions of human gliomas provide so little
detectable prolongation of patient survival? Using these
models to analyze the results of a recent therapeutic
experiment, that conducted by Gutin, et al.,5 one can
calculate that glioblastomas grow twice as rapidly as
anaplastic astrocytomas and that 121 implants in the
wall of the recurrent neoplasms kill about twice as
many generations of both types of tumor as chemother-apy given at the time of recurrence.6

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RESPONSE: Using simple exponential growth curves,
Dr. Alvord has demonstrated the number of doubling
times required for a partially excised tumor to return
to its original volume. This method was also applied to
the shell of an invasive neoplasm following "gross total"
resection.

As pointed out by Dr. Alvord, these models are based
on simple exponential progression and, therefore,
should serve as foundations on which other in vivo
factors may be laid. Those factors that may alter these
growth curves include intratumor as well as host-tumor
interactions. Rates of cell death and cell removal, in
addition to the recruitment or suppression of cells
entering the proliferative pool from the nonproliferative
tumor cell population, will modify expected tumor
doubling times.

Acknowledging the short tumor-doubling times of
invasive malignant gliomas and our inability to remove
100% of these tumors surgically, it is no surprise that
cytoreductive surgery alone in the treatment of these
infiltrative neoplasms has not definitely impacted sur-
vival. As mentioned in previous correspondence,
diagnostic biopsy and the occasional need for surgical de-
compression in symptomatic patients have been the
only historically proven indications for surgery in this
unfortunate patient population.

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Natural History of Symptomatic Brain AVM's

To THE EDITOR: I enjoyed reading the article by
Ondra, et al. (Ondra SL, Troupp H, George ED, et al: The natural history of symptomatic arteriovenous mal-
formations of the brain: a 24-year follow-up assessment.
J Neurosurg 73:387–391, September, 1990). This pa-
tient population is of interest to interventional neuro-
radiologists because the patients had not undergone
surgery, which is similar to the situation in patients
referred for possible endovascular procedures.

The annual rate of bleed or rebleed in this series was
4.0%, which was compared to previously reported inci-
dences of 2% to 3%. It should be noted that two
different methods of calculating the incidence of hem-
orrhage have been used in different series: 1) the person-
year method,1 also used by Ondra, et al., and 2) life-
table analysis.1-3

The person-year method gives the rate of hemorrhage
ever person-year at risk.3 It is simply calculated as fol-
low: rate = n/(Nt), where n is the number of hem-
orrhages, N the number of patients, and t the average
length of follow-up evaluation.
The person-year method and life-table analysis should give similar results; however, the patients who have bled more than once will increase the rate of hemorrhage in the person-year method while life-table analysis looks at survival free of hemorrhage (that is, the patient's first hemorrhage in the follow-up period). For example, one patient in Ondra's series bled 12 times. This would increase the rate of hemorrhage calculated by the person-year method; however, only the first hemorrhage would have been counted in a life-table analysis. If only first hemorrhages are counted when calculating the incidence of hemorrhage with the person-year method, the results of the two analyses are similar. Table 1 shows the rates of hemorrhage in four series of patients, calculated by both methods where possible.

The risk of first hemorrhage in the follow-up period observed by Ondra, et al., is in fact slightly lower than that observed in the series of Crawford, et al. This could be because, as patients bleed or rebleed, there are less patients at risk for first bleed or rebleed in the long follow-up period in the former series.

TABLE 1
Rate of hemorrhage in patients with brain arteriovenous malformations

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Cases</th>
<th>Average Follow-Up Period (yrs)</th>
<th>No. of Bleeds</th>
<th>Rebleed Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total</td>
<td>First</td>
</tr>
<tr>
<td>Graf, et al., 1983*</td>
<td>71</td>
<td>4.8</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Crawford, et al., 1986</td>
<td>103</td>
<td>2†</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Brown, et al., 1988</td>
<td>217</td>
<td>10.4</td>
<td>&gt;102</td>
<td>77</td>
</tr>
<tr>
<td>Ondra, et al., 1990</td>
<td>168</td>
<td>8.2</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td></td>
<td>160</td>
<td>23.7</td>
<td>147</td>
<td>64</td>
</tr>
</tbody>
</table>

* The first set of numbers is for patients who have never bled. The second set is for patients who have presented with a single hemorrhage.
† This number is referred to as both mean (in the abstract) and median (in the text).
‡ The risk in the 1st year was 6%, overall 2%.
§ The risk of at least one hemorrhage at the 10-year follow-up evaluation was 30%, which correlates more closely with the person-year calculation.

References


Shunts for Normal-Pressure Hydrocephalus

To the Editor: I would like to hear the experience of others with regard to ventriculoperitoneal shunts for normal-pressure hydrocephalus. In my practice, I see a fair number of older people with clinically diagnosed normal-pressure hydrocephalus who have positive computerized tomography (CT) or magnetic resonance imaging and radioisotope cisternography.

The problem relates to the use of shunts on these patients. There are several shunts manufactured by Heyer-Schulte and Cordis that are available at various pressures. I have been using the Cordis shunt for several years. Recently, the manufacturers have revised the shunts with medium pressures of 80 to 120 mm Hg and low pressures of 40 to 80 mm Hg. It has been my experience that when we use a medium-pressure shunt, with pressures that were between 50 and 80 mm Hg and are now between 80 and 120 mm Hg, there is some postoperative clinical improvement in the patient; however, repeat CT has shown no change in the size of the ventricular system. Indeed, sometimes there is no improvement at all in the patient. On the other hand, the use of low-pressure shunts has resulted in subdural hygromas.

I have three questions. First, what is the experience of our colleagues who see these patients more often than I, and what type of shunt are they using? Second, is a change in the size of the ventricular system improvement or is just clinical improvement on the part of the patient acceptable? Third, if there is no change in the clinical improvement of the patient and the ventricular system remains the same with medium-