1.1 Principles of Combining External Beam and Brachytherapy

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1 Introduction

External beam therapy and brachytherapy are customarily combined on a physical rather than on a biologic basis. This has been done both as a matter of tradition and because no other system has been unequivocally demonstrated to be superior. The purpose of the present chapter is to evaluate concordances and discordances between various biologic and physical prescription systems.

2 Gy for Gy

In a strictly physical sense, a Gy of external beam therapy is identical to a Gy of brachytherapy in that a specific amount of energy is absorbed within a defined volume. Although the simple addition of dose would appear logical, the biologic effects of external beam are, for a given dose, a function of numerous other parameters, ranging from energy to fractionation to volume. Even if these factors are held constant, the biologic effect of dose is not simply additive: 5 Gy added to 15 Gy does not elicit the same biologic effect as 5 Gy added to 70 Gy.

Nevertheless, the simple addition of physical dose has been empirically verified in the management of a variety of malignancies throughout the body. However, it is important to emphasize that this addition has been established only in these areas in which a wide variety of clinical experience has been accumulated with standard volumes, fraction sizes, and dose rates. Within these limits, for example, the total dose tolerable is 70–80 Gy for vaginal cancer and 80–90 Gy for cervical cancer at point A, varying slightly depending on the proportions of brachytherapy and external beam therapy. A similar though somewhat lower range of doses is traditional in the prescription of head and neck malignancies, whether the boost be given with brachytherapy or with shrinking field external beam therapy. The customary dose prescribed for boosting patients with excisional biopsies of breast cancer is virtually identical whether brachytherapy or external beam is used for boosting.

It is important to emphasize that excellent clinical results have been obtained over decades of experience within very specific limits of both brachytherapy and external beam therapy. External beam fraction size has ranged between 1.7 and 2.0 Gy, while dose rates have typically ranged from 0.30 to 1.00 Gy/h (BARKLEY and FLETCHER 1976). The volume of both external beam therapy and brachytherapy must also be kept within standard limits. When treatment volumes are excessive, increased complications occur.

3 The Linear Quadratic Model

3.1 Dose Rate Effects

The linear quadratic model furnishes a basis for understanding the addition of external beam and
brachytherapy (Barendsen 1982; Thames et al. 1982; Withers 1985). The extrapolated tolerance dose (ETD) is defined as the tolerance dose for an infinite number of very small fractions (Barendsen 1982). The relative effectiveness (RE) of a prescribed dose rate is a function only of the mean half-life of repair of sublethal damage and of the alpha/beta ratio (Barendsen 1982). If a standard tolerance dose of 60 Gy at 0.357 Gy/h is utilized, the relative dose rate effectiveness can be calculated as a function of the alpha/beta ratio (Table I).

If, in turn, these values are normalized to a standard point A dose rate of 0.65 Gy/h, the isodoses of Figs. 1 and 2 are generated. As an example, the 1.00 Gy/h isodose is greater by 1.80/1.52, yielding a biologically greater effective dose rate of 1.18 Gy/h at an alpha/beta ratio of 2.5. Analogously, the effective dose rate at point B is 0.24 Gy/h rather than the physical dose rate of 0.30 Gy/h (i.e., 0.30 Gy/h \times 1.24/1.52).

The implications of these effects can be considered for late responding tissues in Fig. 1, with an alpha/beta ratio of 2.5. The increase from 1.00 to 1.18 Gy/h results in shifting the isodose by only 2 mm. Thus, if two 50-h applications are utilized, an additional 1.8 Gy will be given to a minimally greater volume. This will be of no detectable clinical consequence to the relatively radioresistant adjacent vagina and uterus. The increase in effective dose more laterally will increase by 0.06 Gy/h, giving an additional 6 Gy to a volume that is 6 mm wider. Unless the total dose is close to tolerance, this increment would be very difficult to detect. Any bowel or bladder that is further away will have an even smaller difference in effective dose. Thus, the linear quadratic model implies that the normal tissues of the pelvis will be little affected by dose-rate effects from 0.30 to 1.00 Gy/h.

As shown in Fig. 2, there will be even smaller dose-rate effects for acute reactions and tumors, both of which have greater alpha/beta ratios. Two 50-h applications shift the 1.00 Gy/h isodose by less than a mm, and the effective dose increases by only 1.06. Further laterally, the 0.30 Gy/h isodose shifts by less than 2 mm and by only 0.05 Gy/h. Therefore, it is very unlikely that any clinically detectable effects would occur in either acute reactions or in tumors over the standard range of dose rates.

### Table 1. Dose rate relative effectiveness (RE)

<table>
<thead>
<tr>
<th>RE(0.357)</th>
<th>alpha/beta = 2.5</th>
<th>1.29</th>
<th>1.07</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE(0.30)</td>
<td>alpha/beta = 10.0</td>
<td>1.24</td>
<td>1.06</td>
</tr>
<tr>
<td>RE(0.65)</td>
<td>alpha/beta = 2.5</td>
<td>1.52</td>
<td>1.13</td>
</tr>
<tr>
<td>RE(1.00)</td>
<td>alpha/beta = 10.0</td>
<td>1.80</td>
<td>1.20</td>
</tr>
</tbody>
</table>

#### 3.2 Combination of External Beam and Brachytherapy

The linear quadratic model can also be utilized to combine low dose rate brachytherapy with high dose fractionated external beam therapy. The following example assumes tolerance doses of 60 Gy (0.357 Gy/h) at point A with brachytherapy and 60 Gy at point B with external beam (2 Gy