VIII CONGRESO ALATRO
Asociación Ibero Latinoamericana de Terapia Radiante Oncológica

LIMA - PERÚ

Congreso ALATRO 2022

16 - 18 de Noviembre de 2022

Aspectos Radiobiológicos de la dosis única

Victor Bourel
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ALATRO
Asociación Ibero Latinoamericana de Terapia Radiante Oncológica

ARÁN

Radiobiología en Radioterapia

Conocimiento de los fenómenos físicos y biológicos involucrados en la irradiación de tejido.

Aspecto cualitativo

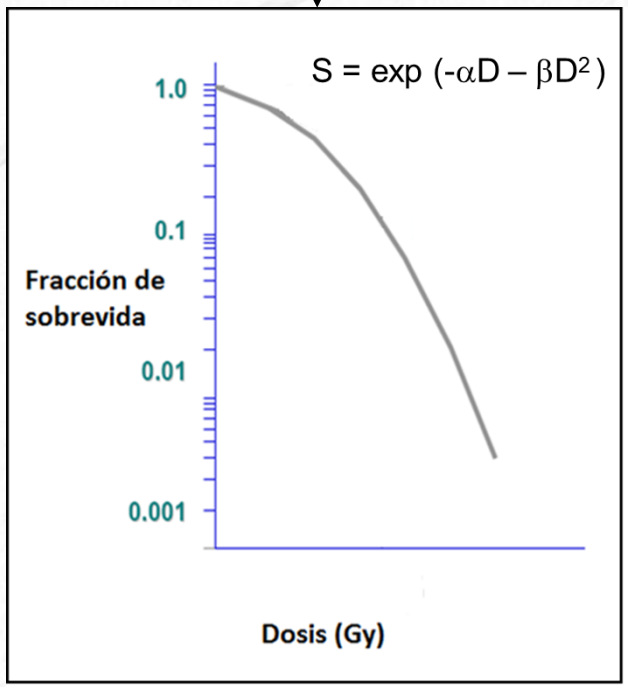
Módelización que refleje los resultados que se obtendrán en la irradiación de tejido

Aspecto cuantitativo

Radiobiología del Fraccionamiento Clásico

5 Rs

- Reparación
- Reoxigenación
- Redistribución
- Repoblación
- Radiosensibilidad



Modelo Lineal Cuadrático

Radiobiología del Fraccionamiento Clásico

5 Rs

- Reparación
- Reoxigenación
- Redistribución
- Repoblación
- Radiosensibilidad

$$BED = n \cdot d \left[1 + \frac{d}{\alpha / \beta} \right]$$

n : número de fracciones
d : dosis por fracción
α/β : parámetro propio de cada tejido

Solo incluye Reparación (puede incluirse Repoblación)

Dosis Biológica Efectiva

Radiobiología del Fraccionamiento Clásico

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- Reparación
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- Redistribución
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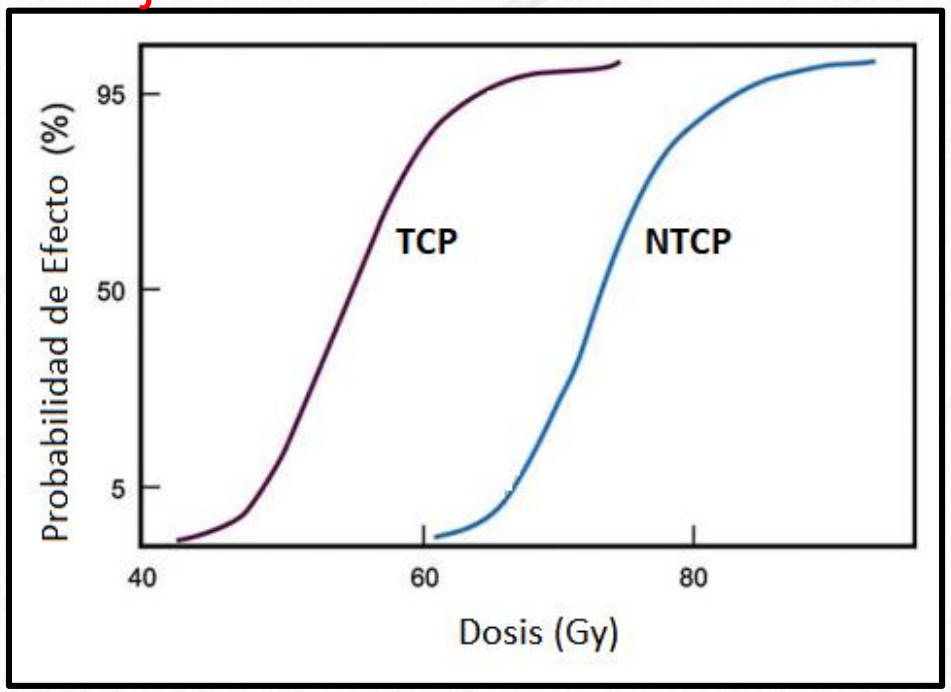
Objetivo final de la modelización



TCP: Tumor Control Probability
NTCP: Normal Tissue Complication Probability

Radiobiología del Fraccionamiento Clásico

5 Rs

- Reparación
- Reoxigenación
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- Radiosensibilidad

$$BED = n \cdot d \left[1 + \frac{d}{\alpha / \beta} \right]$$

Es aplicable en fraccionamientos con altas dosis por fracción ?

Radiobiología de las altas dosis por fracción

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Seminars in
RADIATION
ONCOLOGY

The Linear-Quadratic Model Is Inappropriate to Model High Dose per Fraction Effects in Radiosurgery

John P. Kirkpatrick, MD, PhD, Jeffrey J. Meyer, MD, and Lawrence B. Marks, MD

The linear-quadratic (LQ) model is widely used to model the effect of total dose and dose per fraction in conventionally fractionated radiotherapy. Much of the data used to generate the model are obtained in vitro at doses well below those used in radiosurgery. Clinically, the LQ model often underestimates tumor control observed at radiosurgical doses. The underlying mechanisms implied by the LQ model do not reflect the vascular and stromal damage produced at the high doses per fraction encountered in radiosurgery and ignore the impact of radioresistant subpopulations of cells. The appropriate modeling of both tumor control and normal tissue toxicity in radiosurgery requires the application of emerging understanding of molecular-, cellular-, and tissue-level effects of high-dose/fraction-ionizing radiation and the role of cancer stem cells.

Semin Radiat Oncol 18:240-243

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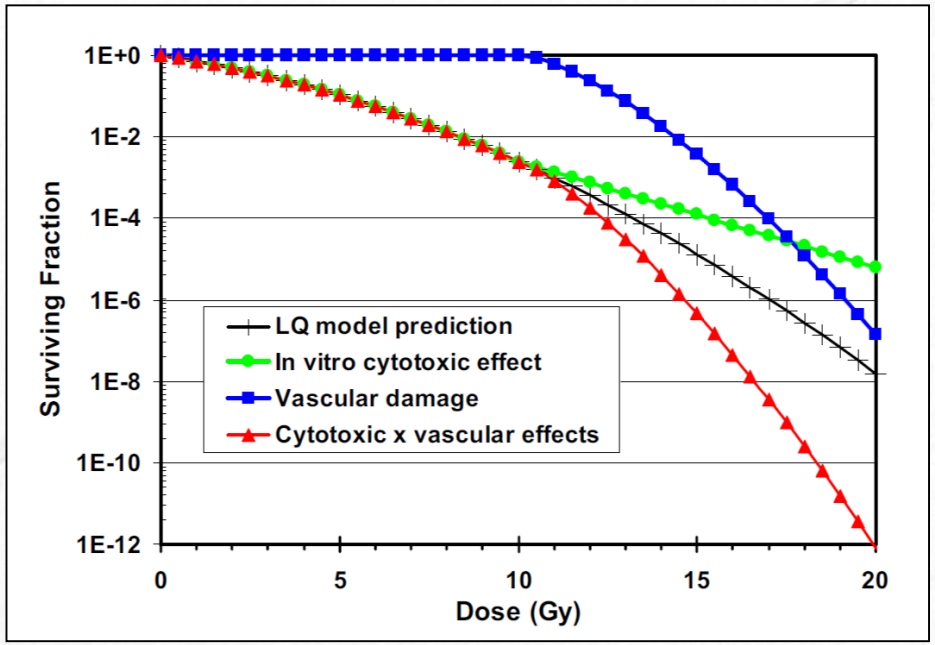
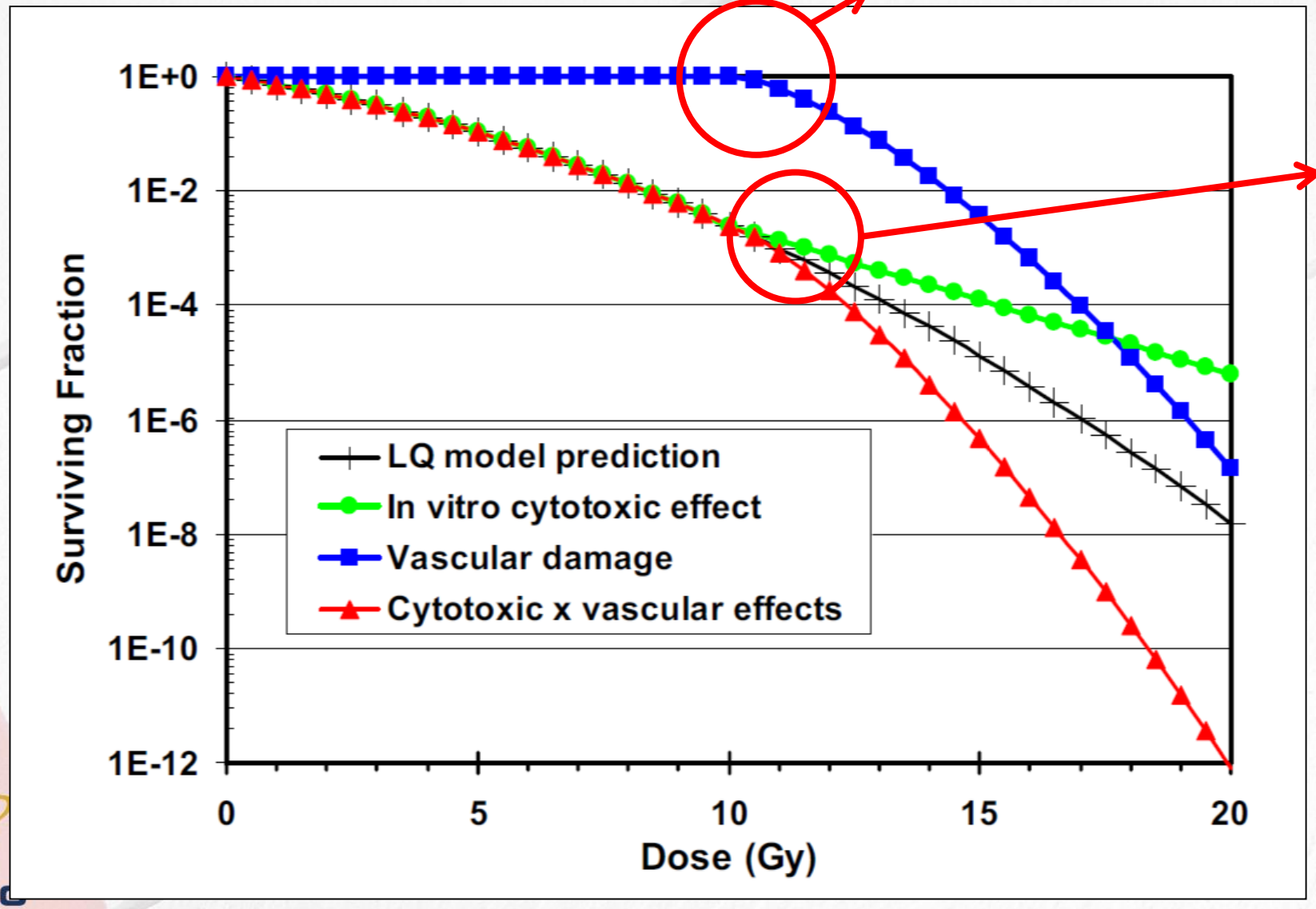


A partir de los 10 Gy en una fracción aparecen los daños vasculares potenciando la muerte celular.



A partir de los 10 Gy en una fracción el modelo Lineal Cuadrático sobrestima el efecto citotóxico.

Radiobiología de las altas dosis por fracción

Therapeutic effects of ablative radiation on local tumor require CD8$^+$ T cells: changing strategies for cancer treatment

*Youjin Lee,[1] *Sogyong L. Auh,[1] Yugang Wang,[1] Byron Burnette,[1] Yang Wang,[1] Yuru Meng,[2] Michael Beckett,[2] Rohit Sharma,[3] Robert Chin,[1] Tony Tu,[1] Ralph R. Weichselbaum,[2] and Yang-Xin Fu[1]

[1]Department of Pathology, [2]Department of Radiation and Cellular Oncology/Ludwig Center for Metastasis Research, and [3]Department of Surgery, University of Chicago, IL

Patients with locally advanced cancer or distant metastasis frequently receive prolonged treatment with chemotherapy and/or fractionated radiotherapy (RT). Despite the initial clinical response, treatment resistance frequently develops and cure in these patients is uncommon. Developments in RT technology allow for the use of high-dose (or ablative) RT to target local tumors, with limited damage to the surrounding normal tissue. We report that reduction of tumor burden after ablative RT depends largely on T-cell responses. Ablative RT dramatically increases T-cell priming in draining lymphoid tissues, leading to reduction/eradication of the primary tumor or distant metastasis in a CD8$^+$ T cell–dependent fashion. We further demonstrate that ablative RT-initiated immune responses and tumor reduction are abrogated by conventional fractionated RT or adjuvant chemotherapy but greatly amplified by local immunotherapy. Our study challenges the rationale for current RT/chemotherapy strategies and highlights the importance of immune activation in preventing tumor relapse. Our findings emphasize the need for new strategies that not only reduce tumor burden but also enhance the role of antitumor immunity. (Blood. 2009;114: 589-595)

BLOOD, 16 JULY 2009 • VOLUME 114, NUMBER 3

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We report that reduction of tumor burden after **ablative RT** depends largely on T-cell responses. **Ablative RT** dramatically increases T-cell priming in draining lymphoid tissues, leading to reduction/eradication of the primary tumor or distant metastasis in a CD8 T cell–dependent fashion.

Critical Review

The Tumor Radiobiology of SRS and SBRT: Are More Than the 5 Rs Involved?

J. Martin Brown, PhD,* David J. Carlson, PhD,† and David J. Brenner, PhD‡

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Stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT), also known as stereotactic ablative radiation therapy (SABR), are rapidly becoming accepted practice for the radiation therapy of certain tumors. Typically, SRS and SBRT involve the delivery of 1 or a few large-dose fractions of 8 to 30 Gy per fraction: a major paradigm shift from radiation therapy practice over the past 90 years, when, with relatively large amounts of normal tissues receiving high doses, the goal was to maximize tumor response for an acceptable level of normal tissue injury. The development of SRS and SBRT have come about because of technologic advances in image guidance and treatment delivery techniques that enable the delivery of large doses to tumors with reduced margins and high gradients outside the target, thereby minimizing doses to surrounding normal tissues. Because the results obtained with SRS and SBRT have been impressive, they have raised the question whether classic radiobiological modeling, and the linear-quadratic (LQ) model, are appropriate for large doses per fraction. In addition to objections to the LQ model, the possibility of additional biological effects resulting from endothelial cell damage, enhanced tumor immunity, or both have been raised to account for the success of SRS and SBRT. In this review, we conclude that the available preclinical and clinical data do not support a need to change the LQ model or to invoke phenomena over and above the classic 5 Rs of radiobiology and radiation therapy, with the likely exception that for some tumors high doses of irradiation may produce enhanced antitumor immunity. Thus, we suggest that for most tumors, the standard radiobiology concepts of the 5 Rs are sufficient to explain the clinical data, and the excellent results obtained from clinical studies are the result of the much larger biologically effective doses that are delivered with SRS and SBRT.

Int J Radiation Oncol Biol Phys, Vol. 88, No. 2, pp. 254–262, 2014

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The Tumor Radiobiology of SRS and SBRT: Are More Than the 5 Rs Involved?

J. Martin Brown, PhD,* David J. Carlson, PhD,† and David J. Brenner, PhD‡

Is the Linear-Quadratic Model Adequate to Describe Cell Killing at High Doses?

Clinical data from prospective randomized trials is of course the gold standard in medicine, but in the absence of good clinical

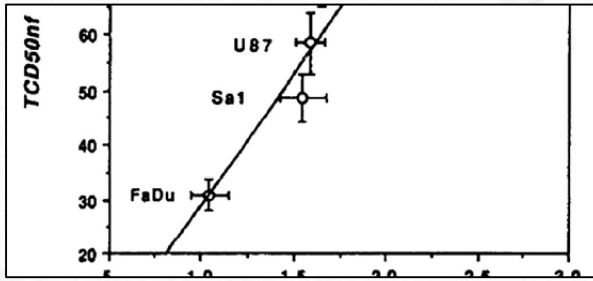
damage to the rat spinal cord (24), for acute damage in mouse skin (25), and for early and late damage to the murine small intestine (26) up to very high single doses. All the quantitative in vivo endpoints are consistent with the LQ model, over a wide range of doses per fraction, including those of interest to SBRT, including the data for single fractions of ~20 Gy. In addition, clinical outcome data for local tumor control can be used to compare biological models over a wide range of doses and frac-

tumor cell kill may not be generally applicable to SBRT.

Vascular damage at high doses produces secondary cell killing

This theory, suggested by Park et al (36), suggests that radiation doses higher than ~10 Gy induce vascular damage leading to

but in this case there was a greater effect of 20 Gy × 1 than of 5 Gy × 4 over 2 weeks. Of interest is that the study in mice (44) and the clinical study with melanoma already mentioned (), the radiation was combined with anti-CTLA-4 antibody; in the case of the preclinical study there was no indication of enhanced antitumor immunity by the radiation alone, although in the study by Lee et al (45), antitumor immunity was achieved by irradiation alone. These data are clearly exciting and illustrate the fact that



tivity of tumors after high dose per fraction radiation therapy.

Enhanced antitumor immunity after tumor irradiation

There is now clinical evidence that for melanoma, irradiation by SBRT of a tumor at 1 site contributes to an antitumor immunologic rejection of a metastatic lesion at a distant site—a so-called abscopal effect (39, 40). So far, the data have been reported for

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Radiobiología de las altas dosis por fracción

En una fracción de alta dosis

1. El modelo Lineal Cuadrático sobrestima la muerte celular
2. Aparece daño vascular potenciando la muerte celular
3. Se potencia el sistema inmunológico anti tumoral

Modificación al Modelo Lineal Cuadrático

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 3, pp. 847–852, 2008

0360-3016/08/$–see front matter

doi:10.1016/j.ijrobp.2007.10.059

BIOLOGY CONTRIBUTION

UNIVERSAL SURVIVAL CURVE AND SINGLE FRACTION EQUIVALENT DOSE: USEFUL TOOLS IN UNDERSTANDING POTENCY OF ABLATIVE RADIOTHERAPY

CLINT PARK, M.D. M.S., LECH PAPIEZ, PH.D., SHICHUAN ZHANG, M.D., PH.D., MICHAEL STORY, PH.D., AND ROBERT D. TIMMERMAN, M.D.

Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX

Purpose: Overprediction of the potency and toxicity of high-dose ablative radiotherapy such as stereotactic body radiotherapy (SBRT) by the linear quadratic (LQ) model led to many clinicians' hesitating to adopt this efficacious and well-tolerated therapeutic option. The aim of this study was to offer an alternative method of analyzing the effect of SBRT by constructing a universal survival curve (USC) that provides superior approximation of the experimentally measured survival curves in the ablative, high-dose range without losing the strengths of the LQ model around the shoulder.

Methods and Materials: The USC was constructed by hybridizing two classic radiobiologic models: the LQ model and the multitarget model. We have assumed that the LQ model gives a good description for conventionally fractionated radiotherapy (CFRT) for the dose to the shoulder. For ablative doses beyond the shoulder, the survival curve is better described as a straight line as predicted by the multitarget model. The USC smoothly interpolates from a parabola predicted by the LQ model to the terminal asymptote of the multitarget model in the high-dose region. From the USC, we derived two equivalence functions, the biologically effective dose and the single fraction equivalent dose for both CFRT and SBRT.

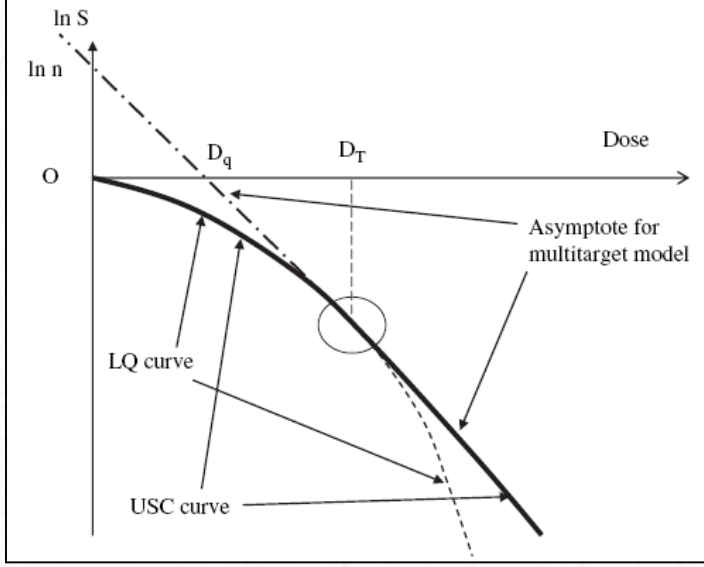
Results: The validity of the USC was tested by using previously published parameters of the LQ and multitarget models for non–small-cell lung cancer cell lines. A comparison of the goodness-of-fit of the LQ and USC models was made to a high-dose survival curve of the H460 non–small-cell lung cancer cell line.

Conclusion: The USC can be used to compare the dose fractionation schemes of both CFRT and SBRT. The USC provides an empirically and a clinically well-justified rationale for SBRT while preserving the strengths of the LQ model for CFRT.

Universal survival curve model

A novel survival curve that hybridizes the LQ model survival curve for the low-dose range and the multitarget model asymptote for high-dose range was constructed (Fig. 2). Doing so takes advantage of the simplicity and superior mechanistic rationale of the LQ model in the low-dose range and the enhanced data fit of the multitarget model in the high-dose range. For continuity there must be a single transition dose (D_T) at which the LQ model smoothly transitions to the terminal asymptote of the multitarget model.

$$\ln S = \begin{cases} -(\alpha \cdot d + \beta \cdot d^2) & \text{if } d \le D_T \quad [5A] \\ -\frac{1}{D_0} d + \frac{D_q}{D_0} & \text{if } d \ge D_T \quad [5B] \end{cases}$$



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Int. J. Radiation Oncology Biol. Phys., Vol. 72, No. 3, pp. 957–959, 2008

0360-3016/08/$–see front matter

LETTERS TO THE EDITOR

LINEAR QUADRATICS IS ALIVE AND WELL: IN REGARD TO PARK *ET AL. (INT J RADIAT ONCOL BIOL PHYS* 2008;70:847–852)

To the Editor: With great respect for Park *et al.* (1, 2), I fear they are on the wrong track in adding a straight log-linear component to a linear quadratic (LQ) curve. If the problem is to simulate a straighter cell-survival curve to higher doses (2, 3), the answer is a simpler and more biologic one and was foreshadowed by Withers and colleagues in 1989 (4).

Tumors that repopulate rapidly are likely to have a greater α/β ratio than 10 Gy (4). Maciejewski *et al.* (4) listed in their Table 3 (p 835) the best-fitting α/β values for squamous cell carcinomas of tongue, oral cavity, tonsil, and buccal mucosa as 25, ∞, 20, and ∞ Gy, respectively. Therefore, to assume an α/β ratio of, *e.g.*, 20 Gy or higher for non–small-cell lung cancer tumors is a reasonable method of solving the alleged geometric problem without throwing the α/β baby out with the bathwater. Straight enough slopes, in that range, eh?

This is a logical expectation from the 1986 lethal-potentially-lethal model of Curtis (5), when the probability of cell death at quick mitosis exceeds the probability of intracellular cell repair in an irradiated population; the ratio of those probabilities determines the α/β ratio. Such a higher α/β ratio has a straighter curve naturally.

It was found in 2000 that non–small-cell lung cancer tumors repopulate approximately as fast as orophangeal tumors (6) and therefore are likely candidates for higher ratios of α/β than 10 Gy. The possibility, assuming $\alpha/\beta = 20$ Gy for comparing fractionation schedules, should be investigated before we need to introduce the ingenious, but awkward, grafting of a straight line onto LQ (1, 2). Figure 1 illustrates the comparison between the straight lines drawn by Park *et al.* (2) and the curves arising from LQ modeling with $\alpha/\beta = 20$ instead of 10 Gy. Differences are small.

The straight (multitarget) cell-survival curves quoted (2) are deceptive because it was shown many years ago that shapes of survival curves at surviving fractions less than 10^{-4} were highly dependent on culture conditions, and when maximum care was used, cell lines with reasonably high extrapolation numbers were curving downward (7), even when often labeled "multitarget." Experimental points always lay below the multitarget straight lines at higher doses. Those intensive discussions that took place in the 1960s and 1970s led to LQ and lethal-potentially-lethal originally; truth does not have a use-by date.

The emphasis on prospectively designed trials (2) is entirely correct. Another useful consequence of $\alpha/\beta = 20$, not 10, is that the estimated effect of repair during long exposures is reduced to one-half (8).

Jack F. Fowler, D.Sc., Ph.D., F.Inst.P.
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doi:10.1016/j.ijrobp.2008.06.1929

1. Park CS, Papiez L, Timmerman R. The unifying (hybrid) survival curve and single fraction equivalent dose: Useful tools in understanding the potency of ablative radiation therapy. Abstract 2767 Proc 49th ASTRO Mtg. *Int J Radiat Oncol Biol Phys* 2007;69(Suppl.):S263–S264.
2. Park CS, Papiez L, Zhang S, *et al.* Universal survival curve and single fraction equivalent dose: Useful tools in understanding potency of ablative radio-therapy. *Int J Radiat Oncol Biol Phys* 2008;70:847–852.
3. Astrahan M. BED calculations for fractions of very high dose: In regard to Park, *et al. (Int J Radiat Oncol Biol Phys* 2007;69:S263–S264*). Int J Radiat Oncol Biol Phys* 2008;71:963–964.
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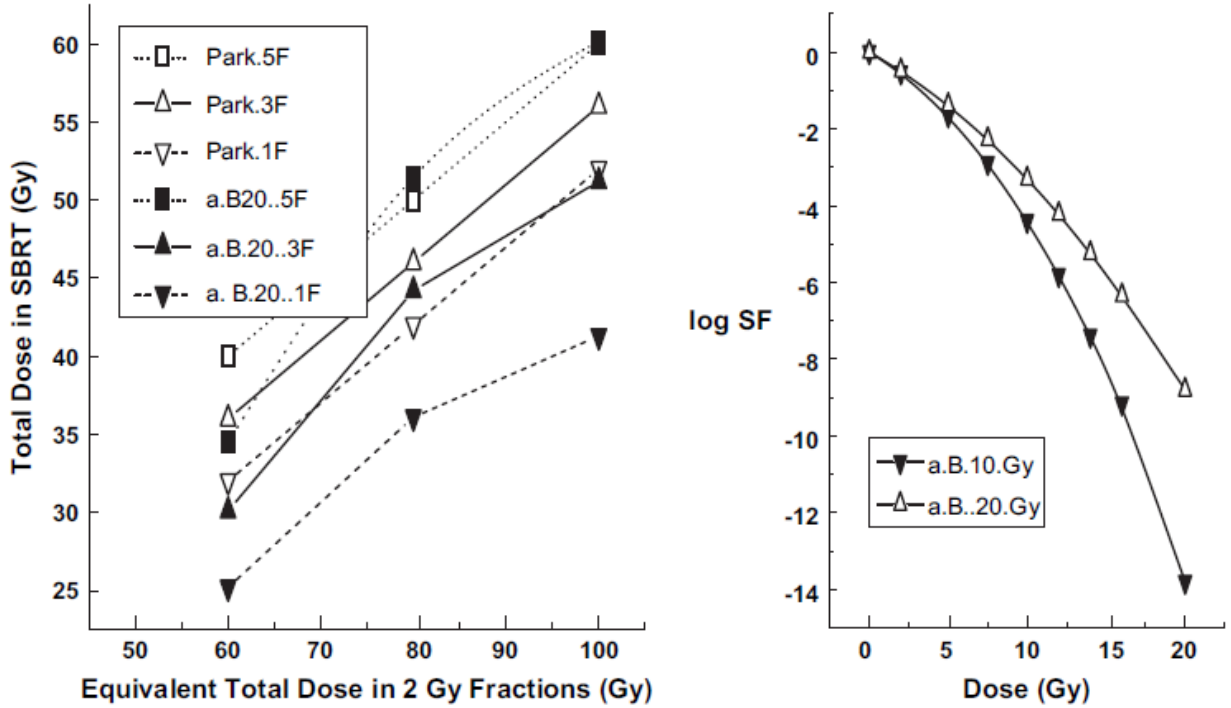

Fig. 1. (Left) Tracing of Fig. 5 in Park *et al.* (2) (open points), with calculated points added (closed points) assuming the $\alpha/\beta = 20$ Gy survival curve (upper in right-hand panel). Differences are interesting, but are not great. SBRT = stereotactic body radiotherapy.

Figure 1 illustrates the comparison between the straight lines drawn by Park *et al.* (2) and the curves arising from LQ modeling with $\alpha/\beta = 20$ instead of 10 Gy. Differences are small.

Modificación al Modelo Lineal Cuadrático

Some implications of linear-quadratic-linear radiation dose-response with regard to hypofractionation

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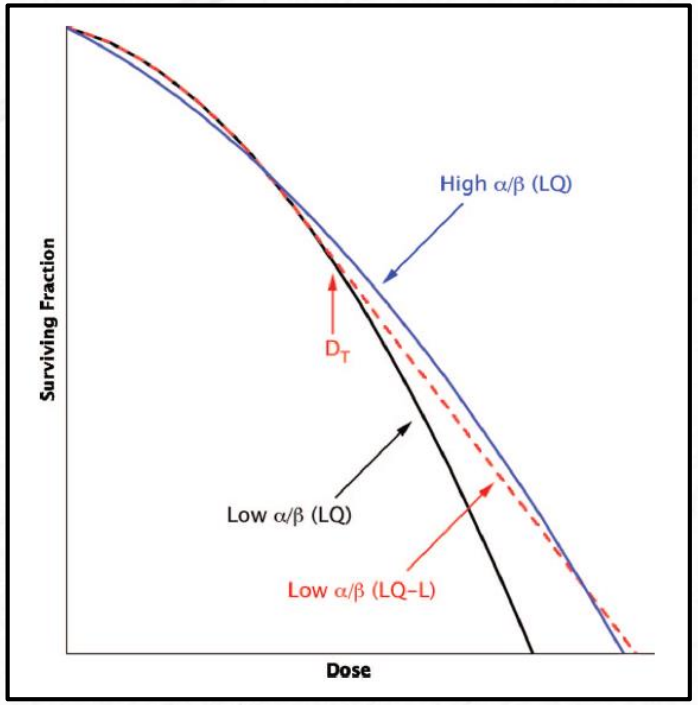
Recent technological advances enable radiation therapy to be delivered in a highly conformal manner to targets located almost anywhere in the body. This capability has renewed the clinical interest in hypofractionation wherein the tumor is delivered a few fractions of very large dose per fraction. Extrapolating clinical experience from conventional regimens to fractions of high dose is important to designing hypofractionated treatments. The concept of biologically effective dose (BED) based on the linear-quadratic (LQ) formulation $e^{-(\alpha D+\beta D^2)}$ is a useful tool for intercomparing conventional fractionations but may be hampered if the value of α/β is dose range dependent and/or when extrapolating to fractions of high dose because the LQ curve bends continuously on the log-linear plot. This does not coincide with what is observed experimentally in many clonogenic cell survival studies at high dose wherein radiation dose-response relationships more closely approximate a straight line. Intercomparison of conventional fractionations with hypofractionated regimens may benefit from BED calculations which instead use a dose range independent linear-quadratic-linear (LQ-L) formulation which better fits the experimental data across a wider range of dose. The dosimetric implications of LQ-L are explored using a simple model which requires only the specification of a dose D_T at which the LQ curve transitions to final linearity and the $\log_e$ cell kill per Gy in the final linear portion of the survival curve at high dose. It is shown that the line tangent to the LQ curve at transition dose D_T can often be used to approximate the final slope of the dose response curve. When $D_T=2\alpha/\beta$ Gy, the line tangent to the LQ curve at D_T intersects the $e^{-\alpha D}$ and $e^{-\beta D^2}$ curves at dose α/β Gy and also closely fits the linear response in the high dose region of some classic *in vitro* cell survival curves for which the value of α/β is low. It is hypothesized that D_T will increase as the magnitude of α/β increases. Examples are presented illustrating how to recognize LQ-L behavior in multifraction isoeffect studies of late responses such as spinal cord and lung. When planning hypofractionated regimens involving reactions with low α/β, recognizing LQ-L behavior could be important because the dose-response is likely to transition to final linearity within the contemplated range of hypofractional doses. © *2008 American Association of Physicists in Medicine*. [DOI: 10.1118/1.2969065]

$$SF = e^{-(\alpha D+\beta D^2)} \quad \text{for } D < D_T$$

and

$$SF = e^{-(\alpha D_T+\beta D_T^2+\gamma(D-D_T))} \quad \text{for } D \geq D_T.$$



Modificación al Modelo Lineal Cuadrático

Mechanistic Repair-Based Padé Linear-Quadratic Model for Cell Response to Radiation Damage

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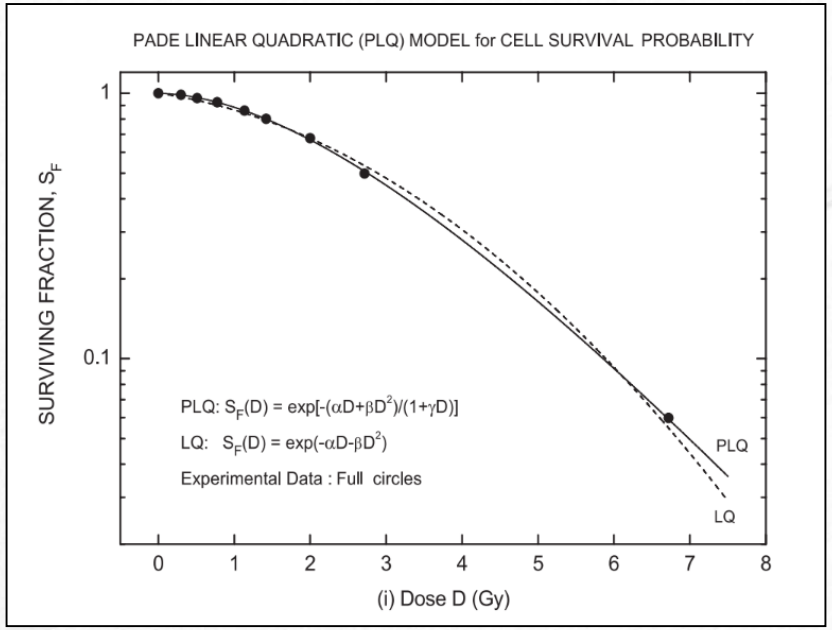
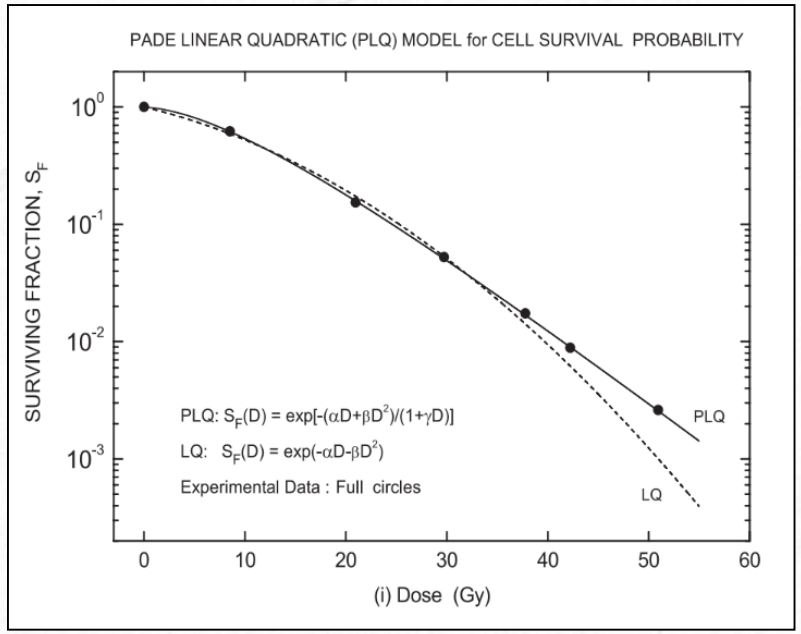
ISSN 0065-3276, http://dx.doi.org/10.1016/B978-0-12-396455-7.00014-5





Irradiación in vitro de celulas humanas de SCLC

Irradiación in vitro de línea V79 de hámster chino

Modelo Lineal cuadrático y sus modificaciones

- **LQ** : Linear Quadratic
- **USC** : Universal Survival Curve
- **LQL** : Linear Quadratic Linear
- **PLQ** : Padé Linear Quadratic

Practical Radiation Oncology (2012) 2, 288–295

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Original Report

Stereotactic body radiation therapy and 3-dimensional conformal radiotherapy for stage I non-small cell lung cancer: A pooled analysis of biological equivalent dose and local control

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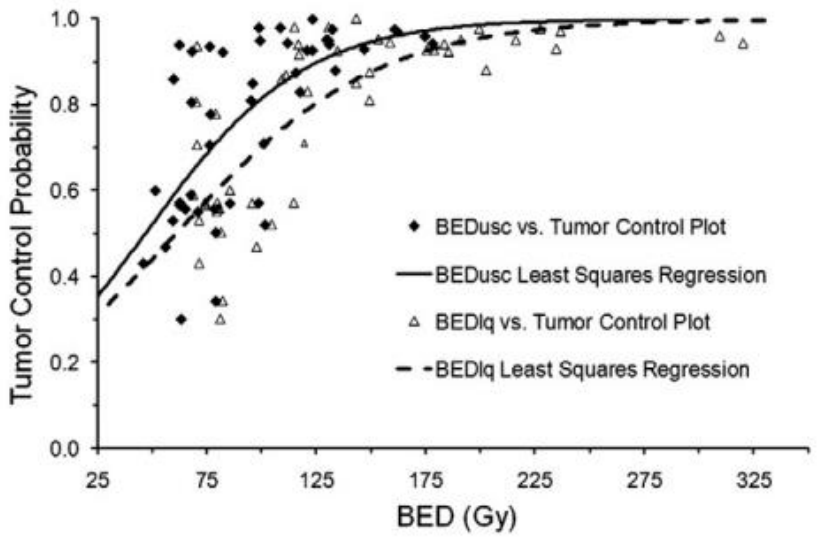

Figure 1 Tumor control probability as a function of the biological equivalent dose (BED) plot for the linear quadratic (LQ) model and the universal survival curve (USC) model as well as their associated least square regression fitted curves.

The USC model differs from the LQ model in predicting BED, but its clinical significance is questionable at higher therapeutic doses required to obtain >90% TC.

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The Tumor Radiobiology of SRS and SBRT: Are More Than the 5 Rs Involved?

J. Martin Brown, PhD,* David J. Carlson, PhD,† and David J. Brenner, PhD‡

Is the Linear-Quadratic Model Adequate to Describe Cell Killing at High Doses?

Clinical data from prospective randomized trials is of course the gold standard in medicine, but in the absence of good clinical

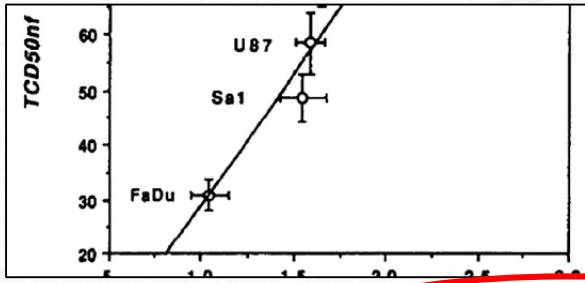
damage to the rat spinal cord (24), for acute damage in mouse skin (25), and for early and late damage to the murine small intestine (26) up to very high single doses. All the quantitative in vivo endpoints are consistent with the LQ model, over a wide range of doses per fraction, including those of interest to SBRT, including the data for single fractions of ~20 Gy. In addition, clinical outcome data for local tumor control can be used to compare biological models over a wide range of doses and frac-

tumor cell kill may not be generally applicable to SBRT.

Vascular damage at high doses produces secondary cell killing

This theory, suggested by Park et al (36), suggests that radiation doses higher than ~10 Gy induce vascular damage leading to

but in this case there was a greater effect of 20 Gy × 1 than of 5 Gy × 4 over 2 weeks. Of interest is that the study in mice (44) and the clinical study with melanoma already mentioned (), the radiation was combined with anti-CTLA-4 antibody; in the case of the preclinical study there was no indication of enhanced antitumor immunity by the radiation alone, although in the study by Lee et al (45), antitumor immunity was achieved by irradiation alone. These data are clearly exciting and illustrate the fact that



tivity of tumors after high dose per fraction radiation therapy.

Enhanced antitumor immunity after tumor irradiation

There is now clinical evidence that for melanoma, irradiation by SBRT of a tumor at 1 site contributes to an antitumor immunologic rejection of a metastatic lesion at a distant site—a so-called abscopal effect (39, 40). So far, the data have been reported for

Clinical Data Suggest That Radiobiological Modeling With the Linear-Quadratic Equation Is Adequate to Explain the Efficacy of SRS and SBRT

In a recent editorial (58), we suggested that dose escalation, not "new biology," can account for the efficacy of SBRT with early-

8. Horiot JC, Le Fur R, N'Guyen T, et al. Hyperfractionation versus conventional fractionation in oropharyngeal carcinoma: Final analysis of a randomized trial of the EORTC cooperative group of radiotherapy. *Radiother Oncol* 1992;25:231-241.
9. Brenner DJ, Hall EJ. Fractionation and protraction for radiotherapy of prostate carcinoma. *Int J Radiat Oncol Biol Phys* 1999;43:1095-1101.
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11. Carlson DJ, Keall PJ, Loo BW Jr., et al. Hypofractionation results in reduced tumor cell kill compared to conventional fractionation for tumors with regions of hypoxia. *Int J Radiat Oncol Biol Phys* 2011;

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Critical Review

The Tumor Radiobiology of SRS and SBRT: Are More Than the 5 Rs Involved?

J. Martin Brown, PhD,* David J. Carlson, PhD,† and David J. Brenner, PhD‡

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In this review, we conclude that the available preclinical and clinical data do not support a need to change the LQ model or to invoke phenomena over and above the classic 5 Rs of radiobiology and radiation therapy,

Stereotactic radiosurgery (SRS) and stereotactic body radiation therapy (SBRT), also known as stereotactic ablative radiation therapy (SABR), are rapidly becoming accepted practice for the radiation therapy of certain tumors. Typically, SRS and SBRT involve the delivery of 1 or a few large-dose fractions of 8 to 30 Gy per fraction: a major paradigm shift from radiation therapy practice over the past 90 years, when, with relatively large amounts of normal tissues receiving high doses, the goal was to maximize tumor response for an acceptable level of normal tissue injury. The development of SRS and SBRT have come about because of technologic advances in image guidance and treatment delivery techniques that enable the delivery of large doses to tumors with reduced margins and high gradients outside the target, thereby minimizing doses to surrounding normal tissues. Because the results obtained with SRS and SBRT have been impressive, they have raised the question whether classic radiobiological modeling, and the linear-quadratic (LQ) model, are appropriate for large doses per fraction. In addition to objections to the LQ model, the possibility of additional biological effects resulting from endothelial cell damage, enhanced tumor immunity, or both have been raised to account for the success of SRS and SBRT. In this review, we conclude that the available preclinical and clinical data do not support a need to change the LQ model or to invoke phenomena over and above the classic 5 Rs of radiobiology and radiation therapy, with the likely exception that for some tumors high doses of irradiation may produce enhanced antitumor immunity. Thus, we suggest that for most tumors, the standard radiobiology concepts of the 5 Rs are sufficient to explain the clinical data, and the excellent results obtained from clinical studies are the result of the much larger biologically effective doses that are delivered with SRS and SBRT. © 2014 Elsevier Inc.

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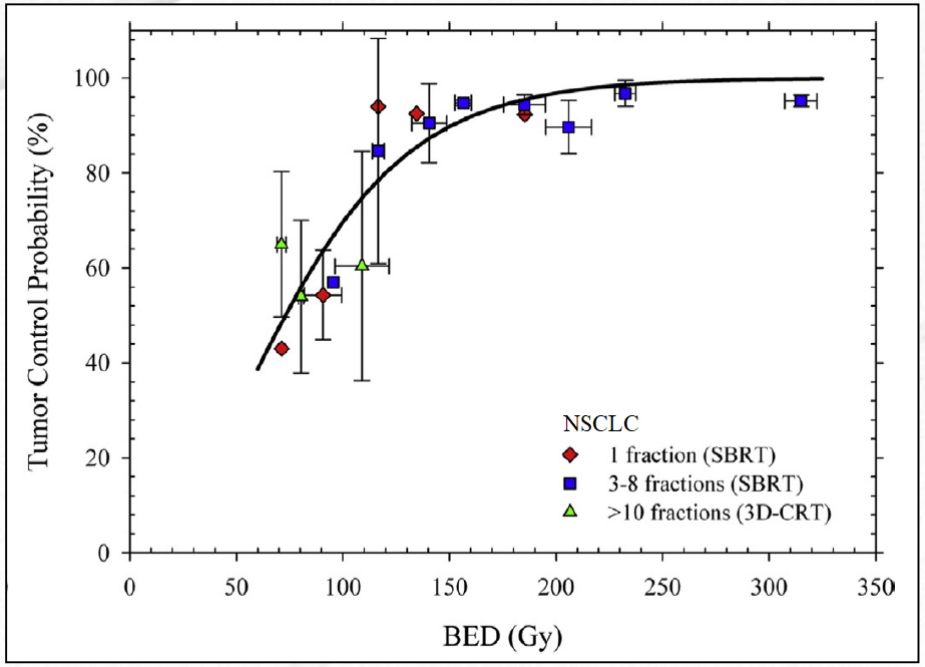

The higher TCPs for SBRT can therefore be fully explained by the much higher tumor doses delivered, and they are entirely consistent with predictions of the LQ model. For NSCLC, there is no need to invoke a "new biology" to explain the high cure rates. We have also reached the same conclusions for brain metastases.

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Original article

High-dose and fractionation effects in stereotactic radiation therapy: Analysis of tumor control data from 2965 patients

Igor Shuryak [a], David J. Carlson [b,*], J. Martin Brown [c], David J. Brenner [a]

[a] *Center for Radiological Research, Columbia University, New York;* [b] *Department of Therapeutic Radiology, Yale University School of Medicine, New Haven; and* [c] *Division of Radiation and Cancer Biology, Department of Radiation Oncology, Stanford University, USA*

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High-dose and fractionation effects in stereotactic radiation therapy: Analysis of tumor control data from 2965 patients

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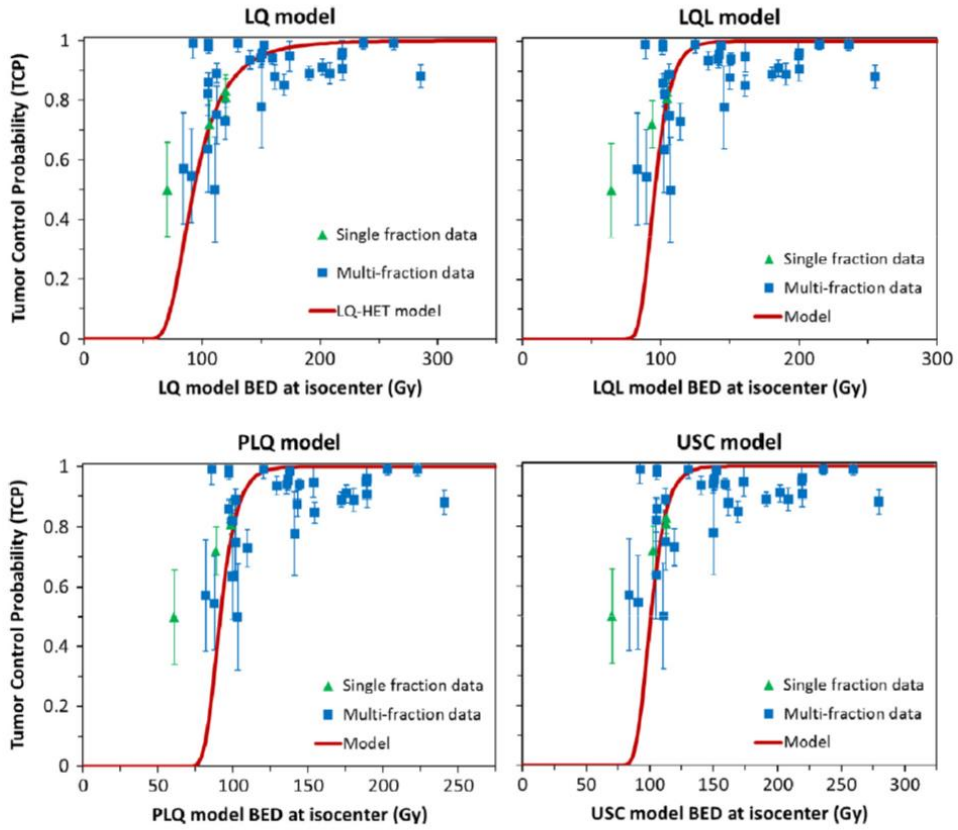

Fig. 1. Best fits to data on early-stage NSCLC from the LQ model with heterogeneous radiosensitivity (LQ), and from the LQL, PLQ and USC models with homogeneous radiosensitivity. In this and the following figures, error bars represent standard errors.

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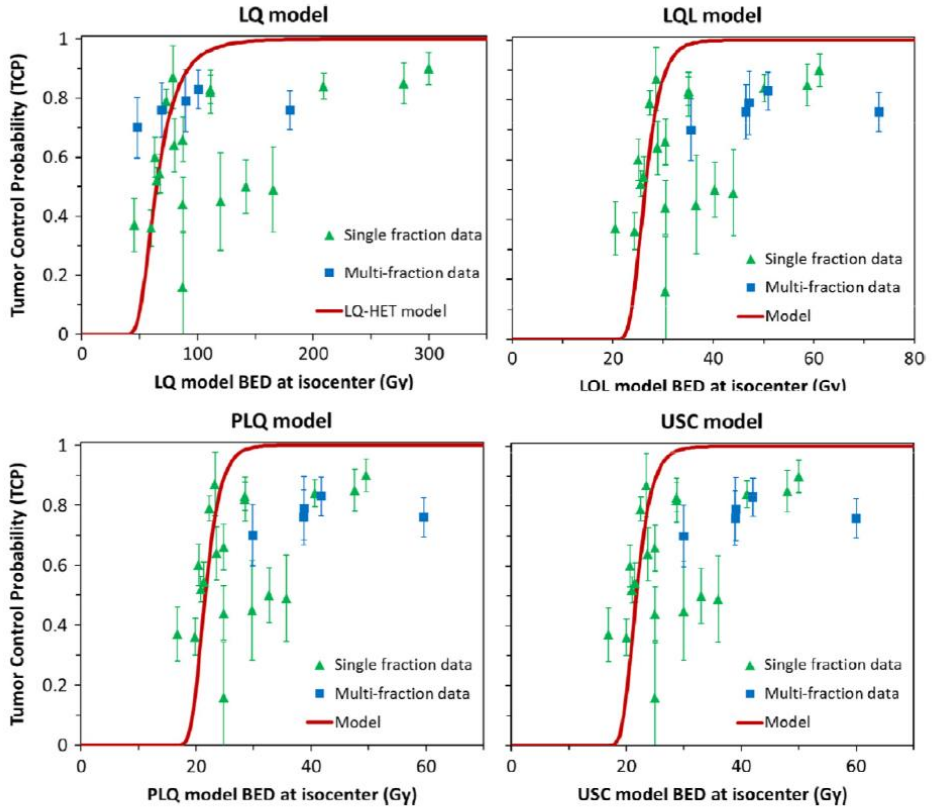

Fig. 2. Best fits to data on brain metastases from the LQ model with heterogeneous radiosensitivity (LQ), and from the LQL, PLQ and USC models with homogeneous radiosensitivity.

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Results

Visual inspection of best-fit predictions from the analyzed models (Figs. 1 and 2) suggests that the LQ model with heterogeneous radiosensitivity provides a much better description of the SRT TCP data as compared with the models (LQL, PLQ and USC) which include an extra high-dose mechanism.

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HyTEC Organ-Specific Paper: Brain and Eye

Tumor Control Probability of Radiosurgery and Fractionated Stereotactic Radiosurgery for Brain Metastases

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Grupo de trabajo de AAPM para evaluar efectos biológicos del hipofraccionamiento.

Se revisaron 56 estudios (13.929 tumores) publicados entre enero 1997 y septiembre 2017.

Equivalencias hasta mas de 20Gy en una fracción (SFED) calculadas con modelo LQ sin modificar con α/β alto obtenido de los datos clínicos de TCP.

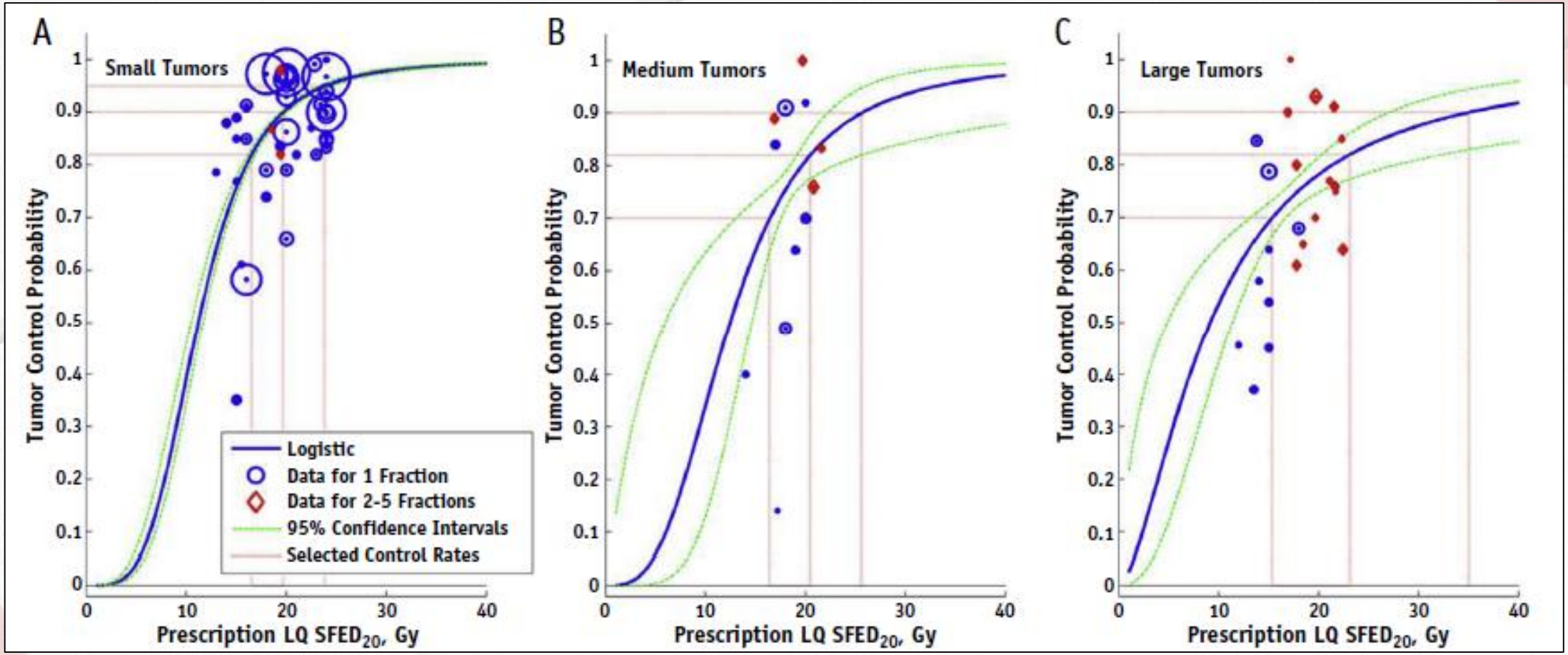
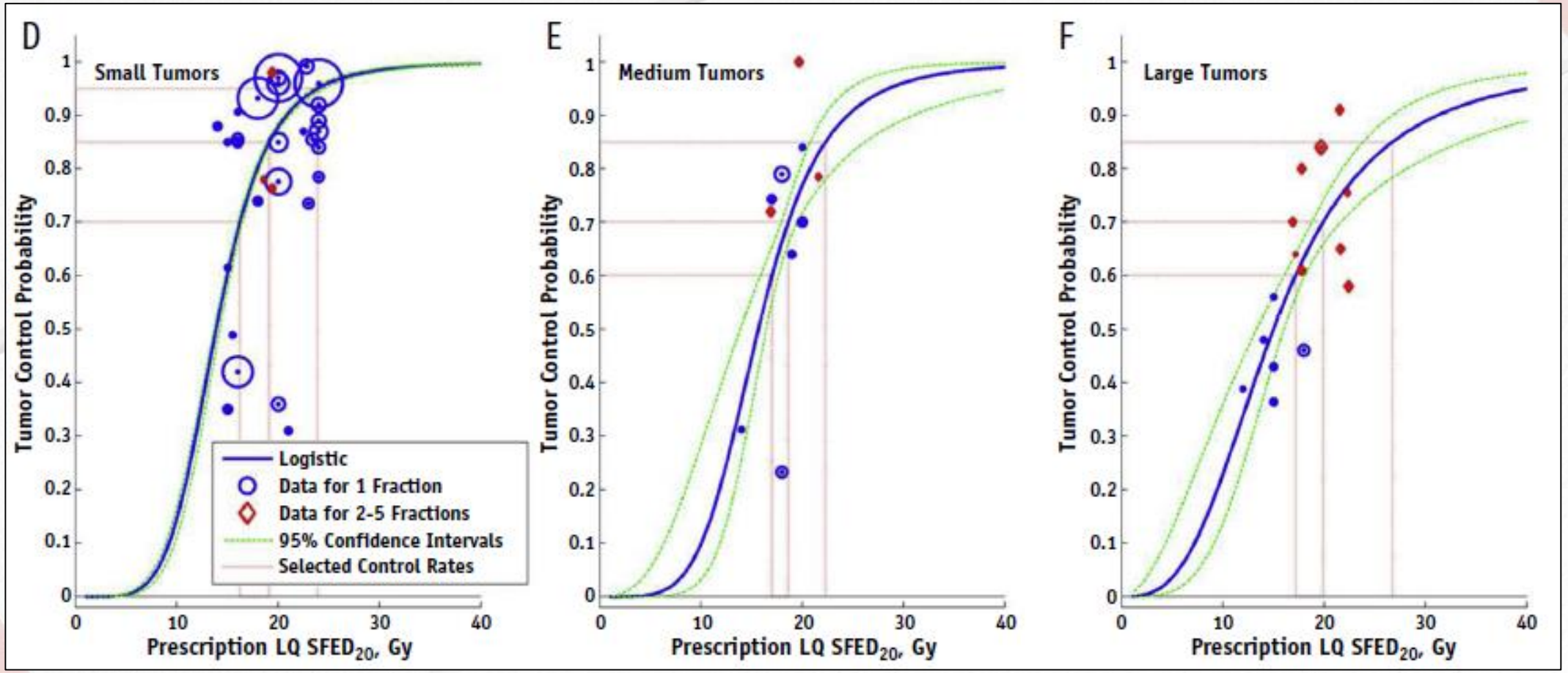


Fig. 2. Logistic models in single-fraction equivalent dose (Gy) with $\alpha/\beta = 20$ Gy, for 1-year local control (A-C) and 2-year local control (D-F), stratified by small, medium, and large tumor size. Note that dose is based on the reported prescribed dose to the planning target volume margin.



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"All models are wrong, but some are useful"

George Box

Conclusiones

1. En tratamientos de fracción única el daño vascular y la mejora de inmunidad radioinducida colaboran positivamente en el control tumoral.
2. La modificación del Modelo LQ a altas dosis hace que pierda su simplicidad y agrega parámetros que no se encuentran evaluados.
3. El Modelo LQ original puede tener buenos resultados en dosis altas con la sola condición de tomar α/β adecuado (generalmente mayor).
4. La modificación del Modelo LQ a altas dosis se muestra mas eficiente para tejidos con α/β pequeño.
5. Los cálculos de TCP utilizando Modelo LQ original muestran excelentes resultados con la condición de utilizar α/β apropiado.

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Congreso ALATRO 2022

16 - 18 de Noviembre de 2022

Muchas gracias

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