ТЕХНІКА ТА МЕТОДИ ЕКСПЕРИМЕНТУ
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ADVANTAGE OF A DYNAMICAL (B/Gd) NEUTRON BEAM CANCER THERAPY OVER A STATIONARY THERAPY

This communication reports on a demonstration that a dynamical neutron beam is superior, in penetrating the surface of a (B/Gd)-loaded cancerous region, to a stationary neutron beam of the same intensity. The reported analysis of this complex problem is based on a one-group neutron diffusion theory with a periodic external neutron beam source in a one-dimensional geometry.

Keywords: neutron diffusion, dynamical neutron source, cancer therapy.

1. Problem formulation

The idea of dynamical neutron cancer therapy in a composite-cancerous region [1, 2], has been dormant as a subject of theoretical physics since 2002. This idea has however started recently [3] to be put into practice, when a time-modulated neutron beam was suggested to function with a variable frequency ω, which serves as a control variable, in a nonlinear optimization process that may extremize some quality indices for this therapy. An optimization process that has recently been extended [4], to the case of dynamical cancer therapy by two opposing neutron beams.

Stationary beams of slow neutrons, produced by reactor sources or accelerators, provide a basis for neutron cancer therapy (NCT), BNCT [5, 6] and/or GdNCT [7]. The beams can, these days, be directed onto malignant tissues, through healthy tissues, using collimators, hollow neutron guides [8] or possibly by solid neutron fibers. These beams can also be dynamic, i.e. temporally modulated by an accelerator. To introduce the subject, consider a space-time thermal neutron flux $\phi(x,t)$ distribution in a B and/or Gd loaded cancerous region R of a thin slab shape, of one-dimensional thickness a, adjacent to a tumor-free region Λ. The diffusion equation for such a flux of one-speed, v, neutrons is known to be

$$\frac{1}{v}\frac{\partial}{\partial t}\phi(x,t) - D\frac{\partial^2}{\partial x^2}\phi(x,t) + \Sigma_a\phi(x,t) = S(x,t),$$

$$0^- \le x \le l, \qquad (1)$$

where $\phi(x,t) = vN(x,t)$ and $N(x, t)$ is the neutron density and 0^- is the limit to 0 from the left.

In the notation of the classical literature on reactor engineering, see e.g. [9 - 11], Σ_a is the macroscopic absorption cross-section of these neutrons in R and D is the corresponding diffusion coefficient. The point $x = 0$ shall be the point of the source application, $x = a$ is the physical boundary of the slab R, while $x = l$ shall be the extrapolated boundary [9 - 11], of R. The source term $S(x, t)$ in (1) is assumed to be discontinuous in x and to emerge from a moderator mounted on an accelerator target that can be modulated in time. The thermal neutron beam is then transported by a system of hollow neutron guides or solid neutron fibers in the region Λ, as illustrated in the Figure. In particular

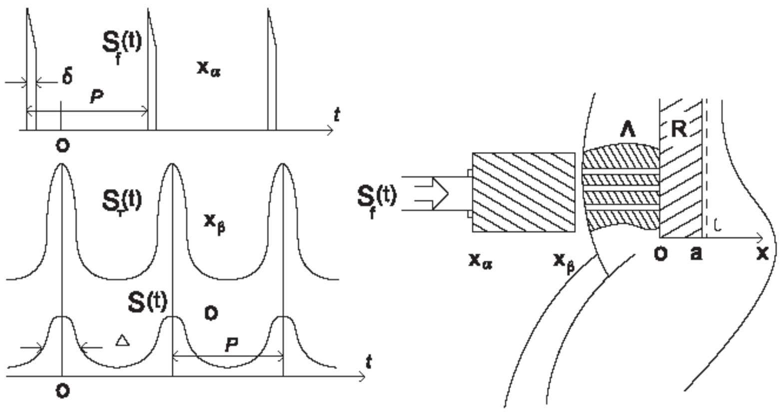
$$S(x,t) = \begin{cases} S(t) = a_0/2 + \sum_{m=1}^{\infty} a_m \cos m\omega t; \ x = 0^-, \\ 0; \ x > 0 \end{cases} \qquad (2)$$

where $S(t)$ is designed as a periodic function, with a period P, of even symmetry (for the sake of simplicity) with a time modulation frequency $\omega = 2\pi/P$, which can be varied, within technical limits, by the accelerator operator.

Such a model for the neutron source assumes that even before the source modulation starts at $t = 0$, a steady-state source (stationary mode) exists with a level equaling to $a_0/2$. This situation is a mathematical reality when using Fourier series representations, which can practically be achieved by a special design of operating the accelerator neutron beam.

A time-modulated thermal neutron beam $S(t)$ with a mean level of $a_0/2$ happens to generate a neutron density wave, see e.g. Haidar [3], that is claimed to penetrate the surface of a B/Gd-loaded finite cancerous region better than a stationary neutron beam of the same $S = a_0/2$ level. *The purpose of this letter is just to demonstrate that this claim is correct.*

It is further anticipated that the deployed accelerator can generate repeated pulses of fast neutrons $S_f(t)$ at x_α of pulse width δ in the range of 10 μs < δ < < 1000 μs. At the end of the moderator, i.e. at x_β, the thermal neutron source becomes $S_T(t)$, as sketched in the Figure.



Sketch to illustrate the accelerator based single dynamical neutron beam.

After transportation through Λ, this same source of thermal neutrons emerges at $x = 0$ with a reduced amplitude as $S(t)$. The width Δ of the resulting peak in this $S(t)$, though proportional to δ, is orders of magnitude larger than δ, see e.g. [12] and [13].

If T_0 is the lifetime of thermal neutrons in R, then therapy in reasonable times requires P to exceed T_0. Hence $T_0 < P << \infty$ i.e.

$$(2\pi/T_0) > \omega >> 0, \quad (3)$$

seems to be a necessary technical constraint in any dynamical NCT.

2. Analyses

It would be assumed throughout this article, that the neutron flux intensity $J(x, t)$ at $x = 0^-$ should satisfy

$$J(0^-, t) = \kappa_{R;\Lambda}\, S(x, t), \quad (4)$$

where $\kappa_{R;\Lambda}$ is a coupling factor between R and the adjacent Λ region.

This may be taken to be

$$\kappa_{R;\Lambda} = \rho_\Lambda/(\rho_R + \rho_\Lambda), \quad (5)$$

with ρ_R and ρ_Λ as the albedo (see, e.g. [14]) for Λ and R respectively. To simplify notation, we shall throughout assume

$$å_m = \kappa_{R;\Lambda}\, a_m,\ m = 0, 1, 2, 3 \ldots \quad (6)$$

to consider first a steady-state neutron diffusional process generated only by the stationary term ($m = 0$ mode) of an acting Neumann boundary condition (BC). This is the natural boundary condition corresponding to the stationary $m = 0$ mode, implying that a steady-state source exists with a level equaling to $\mathring{S} = å_0/2$, even before the source modulation starts at t = 0.

Since $\Sigma_a/D > 0$, then we set $\mu^2 = \Sigma_a/D$ to obtain for the case of $\mathring{S} = å_0/2$ the stationary boundary value problem (BVP) solution [3],

$$N_\gamma(x) = (å_0/(2D\nu\mu))\cdot(\sinh\mu(l-x))/(\cosh\mu l)). \quad (7)$$

Clearly $N_\gamma(0) = (å_0/(2D\nu\mu)) \tanh\mu l$, while $N_\gamma(l) = 0$.

Consider next a dynamical modal BVP for the differential equation (1), with each m-mode in $S(x, t)$ of (2), generating a modal flux $\phi_m(x, t)$ subject to:

(i) $\phi_m(l, t) = 0$,

(ii) $(\partial/\partial x)\phi_m(x, t)|x = 0 = -(å_m/D)\cos m\omega t$,

(iii) $\phi_m(x, 0) = \varphi_m(x)$; $\varphi_0(x) = N_\gamma(x)$, $\varphi_m(x) = 0$, $\forall m \geq 1$.

Assume further that

$$\beta_n = vD(2n-1)^2(\pi^2/4l^2) + v\Sigma_a, \quad (8)$$

and

$$Q_n(x) = \cos(2n-1)(\pi/2)(x/l), \quad (9)$$

to obtain an analytical solution $N(x, t) = \sum_{m=1}^{\infty} \phi_m(x, t)/v$ to the previous BVP's, which happens remarkably to be decomposable [3], into three superimposed distinct effects viz

$$N(x, t) = N_\rho(x, t) + N_\sigma(x, t) + N_\gamma(x), \quad (10)$$

where $N_\rho(x, t)$ is periodic "dispersive", $N_\sigma(x, t)$ is dissipative and $N_\gamma(x)$ is stationary. These are namely:

$$N_\rho(x, t) = (2/l)\sum_{m=1}^{\infty} å_m \sum_{n=1}^{\infty}\left[\{\beta n \cos m\omega t + m\omega \sin m\omega t\}/\left(\beta_n^2 + m^2\omega^2\right)\right]Q_n(x), \quad (11)$$

$$N_\sigma(x, t) = -(2/l)\sum_{m=1}^{\infty} å_m \sum_{n=1}^{\infty}\left[\beta n/\left(\beta_n^2 + m^2\omega^2\right)\right]e^{-\beta nt}Q_n(x), \quad (12)$$

and $N_\gamma(x)$ is the same as (7).

To perform a reasonable comparison between (10) and (7), consider the simplest possible form for $S(t)$, that is a periodically recurring impulse of duration σ, with amplitude h, which can be defined over one period $P = 2T$ by

$$S(t) = \begin{Bmatrix} h; -\sigma/2 < t < \sigma/2 \\ 0; -T < t < -\sigma/2 \\ 0; \sigma/2 < t < T \end{Bmatrix}. \qquad (13)$$

The pertaining

$$a_m = (2/T)\int_0^T S(t)\cos m\omega t\, dt =$$

$$= (2h/\pi)\int_0^{\sigma/2} \cos m\omega t\, dt$$

generates the line spectrum

$$a_m = (2h/\pi)\sigma\omega\, Sinc(\sigma/2)\omega m, \qquad (14)$$

for which $a_0 = (h/\pi)\sigma\omega$, $a_1 = (h/\pi)\sigma\omega\ Sinc\ (\sigma/2)\omega$, $a_2 = (h/\pi)\sigma\omega\ Sinc\ \sigma\omega$, etc. For any value of ω, the first zero of this spectrum occurs when $(\sigma/2)\omega m = 2.6$, i.e. when

$$m = 5.2/\sigma\omega. \qquad (15)$$

3. Results

Hence if in relation (10) it is desired to truncate m above 1 = M, then it is required to consider in (15) $m = 2$, and this means a design ω satisfying

$$\omega = 2.6/\sigma, \qquad (16)$$

for which

$$a_0 = 2.6\ (h/\pi),$$

$$a_1 = a_M = 2.6\ (h/\pi)\sigma\omega\ Sinc\ 1.3 = 1.407\ (h/\pi),$$

$$a_2 = 0, \quad a_3 < 0, \qquad (17)$$

and a_m is oscillatory for $m \geq 3$. If we additionally truncate n above 3 = N, then (10) takes the form

$$N(x,t) \approx (2/l)\mathring{a}_1 \sum_{n=1}^{3}\left[\{\beta_n \cos m\omega t + m\omega \sin m\omega t\} - \beta_n e^{-\beta n\, t}\right]/\left(\beta_n^2 + \omega^2\right)]Q_n(x) + N_\gamma(x), \qquad (18)$$

with $\mathring{a}_1 = \kappa_{R;\Lambda}\, a_1$ and $\mathring{a}_0 = \kappa_{R;\Lambda}\, a_0$. Further substitution of (16) - (17) in (18) leads to

$$N(x,t) \approx (2.814/\pi)\kappa_{R;\Lambda}(\sigma h/l) \times$$

$$\times \sum_{n=1}^{3}\left(\left\{\sigma\beta_n\left[\cos(2.6/\sigma)t - e^{-\beta n\, t}\right] + 2.6\sin(2.6/\sigma)t\right\}/\left(\sigma^2\beta_n^2 + (2.6)^2\right)\right) \times$$

$$\times Q_n(x) + N_\gamma(x). \qquad (19)$$

Moreover, consideration of

$$C_n = \sigma\beta_n/(\sigma^2\beta_n^2 + (2.6)^2), \qquad (20)$$

in (19) allows for rewriting it as

$$N(x,t) - N_\gamma(t) \approx \frac{2.814}{\pi}\kappa_{R;\Lambda}\sum_{n=1}^{3}$$

$$C_n\left[\cos\frac{2.6}{\sigma}t + \frac{2.6}{\sigma\beta n}\sin\frac{2.6}{\sigma}t - e^{-\beta nt}\right]Q_n(x) \qquad (21)$$

with the trigonometric functions representing a non-symmetric periodic time signal of period

$$\tau = \frac{2\pi}{2.6}\sigma. \qquad (22)$$

Now we can directly analyze relation (21) for some characteristic time moments, starting with $t = 0$, for which

$$N(x,0) - N_\gamma(0) \approx 0. \qquad (23)$$

For $t = \sigma$ and rather small σ, we may consider $e^{-\beta n\sigma} = 1 - \beta_n\sigma$, together with $\sin 2.6 \approx \frac{1}{2}$ and $\cos 2.6 \approx -\frac{\sqrt{3}}{2}$ to arrive at

$$N(x,\sigma) - N_\gamma(\sigma) \approx \frac{2.814}{\pi}\kappa_{R;\Lambda}\sum_{n=1}^{3}$$

$$C_n\left[\frac{1}{2}\cdot\frac{2.6}{\sigma\beta n} + \sigma\beta n - \left(1 + \frac{\sqrt{3}}{2}\right)\right]Q_n(x) \qquad (24)$$

which is a positive quantity (especially for small β_n) multiplied by a, concave in x, $Q_n(x)$ function.

Then asymptotically as $t \to \infty$, i.e. when $e^{-\beta nt} \to 0$, if $t = \infty$ is replaced, for definiteness, by $t = \infty\tau$, then $\cos\frac{2.6}{\sigma}(\infty) = \cos\frac{2.6}{\sigma}(\infty\tau) = \cos\infty(2\pi) = 1$, is paired to $\sin\frac{2.6}{\sigma}(\infty)= \sin\frac{2.6}{\sigma}(\omega\tau)=\sin\infty(2\pi)=0.$

Consequently, $N(x,\infty)-N_\gamma(\infty)\approx\frac{2.814}{\pi}\kappa_{R;\Lambda}\sum_{n=1}^{3} C_n Q_n(x)$, appears also not to be insignificant.

Since $\beta_1 < \beta_2 < \beta_3$, then the first term in (19) is the most dominant term, with $Q_1(x) = \cos(\pi/2)(x/l)$, as a concave function with a peak at $x = 0$ and a node at $x = l$. The second term (less significant) is with $Q_2(x) = \cos3(\pi/2)(x/l)$, which is also concave between its peak at $x = 0$ and its first node at $x = l/3$. It becomes however negative over the $(l/3, l)$ interval. Then the third term (the least significant) is with $Q_3(x) = \cos5(\pi/2)(x/l)$, which is also concave between its peak at $x = 0$ and its first node at $x = l/5$. It is also negative over the $(l/5, l)$ interval.

Clearly, $N(x,t)$ for $t > 0$ is a superposition of the above three concave functions over the $N_\gamma(x)$ convex function having a minimum at $x = l$. Moreover, $N(x,t) > N_\gamma(x)$ at least for $0 < x < l/5$. Moreover, approximately quantitatively, for $0 < x < l/5$, $[N(x,t) - N_\gamma(x)] \sim hl^3/(\nu\Sigma_a)^2$, and is practically independent of σ, when $\omega = 2.6/\sigma$. This difference is traded off by the possibility for $N(x,t) < N_\gamma(x)$ for $l/5 < x < l$. We may conclude therefore that a dynamic neutron beam has a superior penetration, of the surface of a cancerous region, to a static neutron beam of the same intensity. Deep inside the cancerous region, however, the situation is qualitatively reversed, but with slower spatial variation though. This fact motivates and justifies the argument for dynamical cancer therapy with two opposing neutron beams [15], or with three mutually orthogonal neutron beams [16]. Furthermore, it should be noted that this neutronic behavior happens to be consistent with the existence of an optimal [4], beam frequency that extremizes the utility and ballistic therapeutic indices [3, 4], of the dynamical neutron flux.

4. Conclusion

In conclusion, this letter demonstrates in the simplest possible way, a widely incomprehensible reason for enhancing neutron spatial penetration by temporal modulation. The mechanism is indeed that of a neutron-density wave. A neutron-density wave [3, 16], though similar to an acoustic wave, is entirely different from it. An acoustic wave is essentially an eigensolution to a homogeneous hyperbolic PDE, whereas a neutron-density wave is a Duhammel's solution to a nonhomogeneous parabolic PDE, with exclusively a harmonic external source.

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ПЕРЕВАГА ДИНАМІЧНОЇ (B/Gd) НЕЙТРОННОЇ ТЕРАПІЇ РАКУ НАД СТАЦІОНАРНОЮ ТЕРАПІЄЮ

Демонструється перевага динамічного нейтронного пучка над стаціонарним пучком нейтронів тієї ж інтенсивності при проникненні в онкологічну область, завантажену бором та/або гадолінієм (B/Gd). Проведений аналіз цієї складної проблеми ґрунтується на одногруповій теорії нейтронної дифузії з періодичним зовнішнім пучком нейтронів в одновимірній геометрії.

Ключові слова: нейтронна дифузія, динамічне джерело нейтронів, терапія раку.

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ПРЕИМУЩЕСТВО ДИНАМИЧЕСКОЙ (B/Gd) НЕЙТРОННОЙ ТЕРАПИИ РАКА НАД СТАЦИОНАРНОЙ ТЕРАПИЕЙ

Демонстрируется преимущество динамического нейтронного пучка над стационарным пучком нейтронов той же интенсивности при проникновении в онкологическую область, загруженную бором и/или гадолинием (B/Gd). Проведенный анализ этой сложной проблемы основывается на одногрупповой теории нейтронной диффузии с периодическим внешним пучком нейтронов в одномерной геометрии.

Ключевые слова: нейтронная диффузия, динамический источник нейтронов, терапия рака.

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