

Relationship between Rehabilitation Therapies and Outcome of Stroke Patients in Israel: A Preliminary Study

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Abstract

Background: The relationship between the amount of rehabilitation therapy and functional outcome in stroke patients has not been established.

Objectives: To evaluate the effectiveness of inpatient rehabilitation for post-acute stroke, and examine the relationship between intensity of therapies and functional status at discharge.

Methods: We evaluated 50 first-stroke patients, average age 63 years, in a prospective descriptive study. The impairment and Functional Independence Measurement were assessed both at admission to rehabilitation and at discharge. Patients were monitored weekly during their stay by means of discipline-specific measures of activity level. Predictor variables included intensity of physical, occupational and speech therapies; demographic characteristics; length of stay; and time since the stroke.

Results: A significant reduction in impairment was observed at discharge. The predictors of gains and activity level at discharge as well as motor vs. cognitive components of the FIM were neither consistent nor did they occur in the same trend of functional improvement. Greater FIM motor level at discharge was associated with younger age, higher admission motor and cognitive level, and receipt of any speech therapy, while greater FIM cognitive level was associated with higher cognitive level at admission, shorter interval from onset to admission, and more intense occupational therapy. More intense OT was associated with greater and more cognitive improvement during the hospitalization.

Conclusion: Since the sample was relatively small and heterogeneous in terms of the patients' functional abilities, the findings cannot be generalized to the whole population of stroke patients. Further efforts to identify the best timing, modalities, intensity and frequency of the various treatments are needed to improve the cost-benefit equation of rehabilitation in stroke patients.

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For Editorial see page 772

Rehabilitation clinicians and researchers have long struggled with the fundamental question: To what extent does rehabilitation intervention improve the functional status of patients? The answer

to this question is sought not only by rehabilitation therapists, but also by the payers such as health management organizations (sick funds), insurance companies, etc., to enable them to estimate the cost and benefits of rehabilitation. Distinguishing the benefits of therapy from "spontaneous" neurologic recovery would require randomized trials after the onset of disability, but organizing this type of trial is difficult. Other types of evidence support the efficacy of rehabilitation provided during inpatient hospitalizations. For example, the Copenhagen Stroke Study [1,2] prospectively followed 1,197 patients after acute stroke, and concluded that a reliable prognosis might be expected in all stroke patients within 12 weeks from stroke onset and with limited neurologic and functional recovery after the first 5 months.

Only a few studies have examined the relationship between functional outcome and the timing, duration and intensity of rehabilitation therapies following stroke. Accordingly, the purpose of the present study was to evaluate therapy-outcome relationships in a cohort of stroke patients in Israel, a nation with a generally universal healthcare coverage and longer acute and rehabilitation lengths of stay, as compared to the United States.

Patients and Methods

Patients

Data were collected from 50 stroke inpatients from September 1997 through May 1998 who were hospitalized at the Loewenstein Rehabilitation Hospital in Raanana, Israel. Patients in this facility are referred from general hospitals across the country and reflect diverse socio-cultural-religious backgrounds. Each year about 520 patients are admitted for rehabilitation after a first or recurrent stroke.

Inclusion criteria included: a) first-ever stroke, b) stroke confirmed by neuroimaging (brain computerized tomography scan and/or magnetic resonance imaging), and c) age older than 18 years. Exclusion criteria included: a) length of stay less than 2 weeks, and b) transfer out of rehabilitation for more than 30 days.

Men comprised 64% of the sample and 74% of the sample population was married. The median age was 63 years (range 39–83 years). The median interval from onset of stroke to admission to rehabilitation was 14 days (range 3–51 days). The median length of stay was 83 days (range 27–175). Most patients (96%) were admitted

FIM = Functional Independence Measurement
OT = occupational therapy

from the acute unit of another facility; the others were admitted from home. Mean total Functional Independence Measurement score was 72 (range 18–122) on admission and 101 (range 20–126) at discharge.

Instruments

Impairment measures reflect the myriad aspects of stroke. We used the Mini Mental State Examination [3], the Stroke Impairment Assessment Set [4], and the National Institutes of Health Stroke Scale [5]. These measures were assessed at admission and at discharge.

Activity level was quantified using the Functional Independence Measure [6]. FIM scores were recorded weekly throughout each patient's stay. Rating scale analysis of the FIM instrument has shown that it contains two subsets of items: a measure of motor function and a measure of cognitive function [7]. These two measures were used separately in subsequent analyses.

Discipline-specific activity measures were defined in terms of functional activities from the FIM instrument and the Rehabilitation Institute of Chicago Functional Assessment Scale, a measure that includes a broad range of activities [8]. An advisory board comprising practicing clinicians and supervisors reviewed the draft lists of functional activities and offered suggestions for revisions. Each discipline-specific measure assessed admission status, functional goals and discharge status.

The 10 items comprising the physical therapy measure included several FIM items (mobility, stair climbing, and bed, tub and toilet transfer). The mobility item from the FIM was split into three separate components (walking, powered and manual wheelchair propulsion). Additional RIC-FAS items assessed car and floor transfers and bed mobility.

The 15 items comprising the occupational therapy measure included nine items from the FIM (eating, bathing, grooming, toileting, upper and lower extremity dressing, and bed, tub and toilet transfers) along with RIC-FAS items assessing community integration, leisure/work, financial management, home maintenance, and functional communication.

The 15 items comprising the speech therapy measure included two FIM items (memory, problem solving) as well as RIC-FAS modality-specific expression (oral, written) and comprehension (auditory, reading) items. Other RIC-FAS items were speech production; chewing and swallowing; money management; alternative/augmentative communication; functional communication; alertness, attention, and concentration; orientation; and gestural communication/pragmatics.

Discharge goals were defined by occupational, physical and speech therapists at admission and discharge. Using the discipline-specific functional measures, goal attainment was defined as meeting or exceeding the goal set at admission. Thus, goal attainment was a dichotomous variable, i.e., discharge measure equals or exceeds goal, or is less than goal.

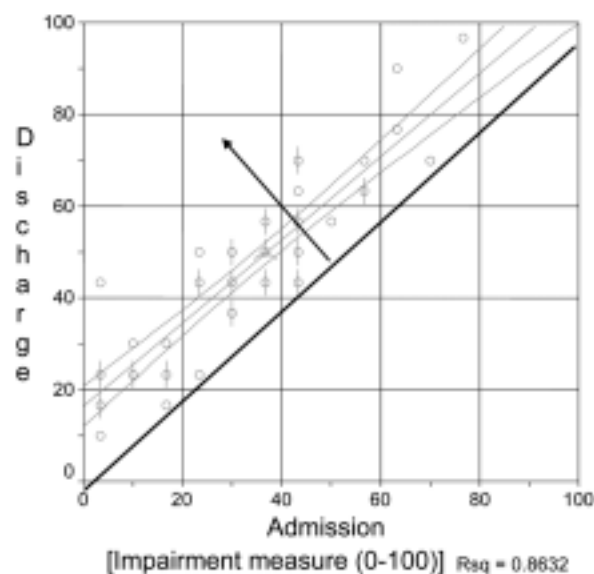


Figure 1. Impairment Change. Sunflower plots show the number of patients at each point. Cases on the bold diagonal (identity) line had the same measure at admission and discharge; cases above the line improved (had reduced impairment at discharge). The best-fit line and 95% confidence interval are shown above the identity line.

Results

Discharge to home was achieved by 78% of the sample; others were discharged to other rehabilitation facilities (14%), skilled nursing facilities (4%) or chronic hospitals (4%). Listed below are the hypotheses that guided this study, together with results of the statistical analyses.

- *Impairment improves significantly from admission to discharge*

A paired sample *t*-test was used to describe improvement in impairment from admission to discharge. Figure 1 shows that impairment improved from admission ($x = 34.8$) to discharge [$x = 48.0$; t ($df = 48$) = 11.1, $P < 0.001$]. The two measures were strongly correlated (0.93).

- *Improvements in impairment severity are not related to therapy intensity*

Figure 2A shows the distribution of occupational therapy intensity, Figure 2B the distribution of physical therapy, and Figure 2C the distribution of speech/language therapy. Non-parametric (Spearman) correlations were used to describe the association between improvement in impairment with intensities of OT, PT and ST (total number of 15 minute units/length of stay in days = units per day intensity). The correlations between therapy intensity and impairment improvement were as follow: for OT [$r = -0.194$; P (two-tailed) = 0.186 while N was 48], for PT [$r = -0.078$, P (two-tailed) = 0.596 while N was 49], and for ST [$r = -0.006$, P (two-tailed) = 0.986 while N was 13]; thus, none of the correlations were statistically

PT = physical therapy
ST = speech therapy

RIC-FAS = Rehabilitation Institute of Chicago Functional Assessment Scale

Quarter hour units per day

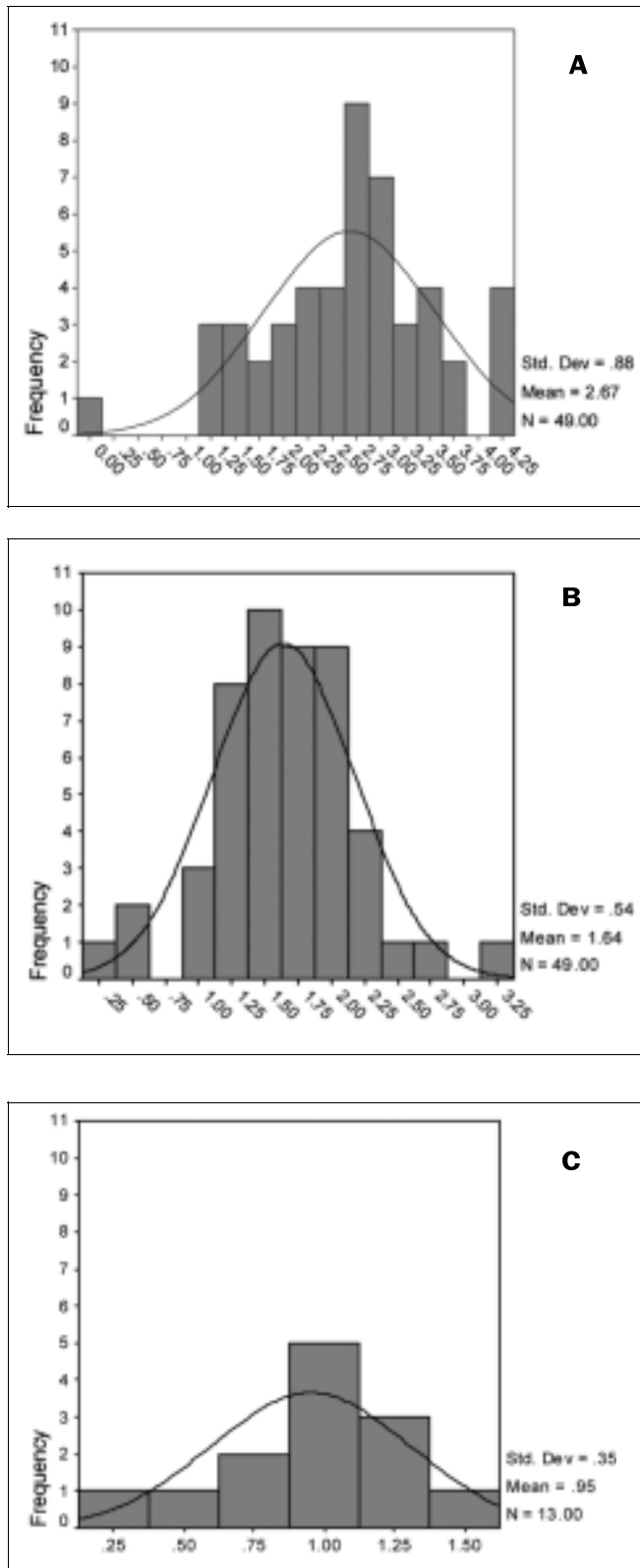


Figure 2. The distribution of therapy intensity in quarter-hour units with an overlaid normal distribution is shown for: **[A]** occupational therapy, **[B]** physical therapy, and **[C]** speech/language pathology therapy.

Table 1. Therapy intensity and disability gains

	OT intensity	PT intensity	ST intensity
FIM Motor gain			
<i>r</i>	0.292*	-0.040	0.041
<i>P</i> (two-tailed)	0.044	0.785	0.895
<i>N</i>	48	49	13
FIM Cognitive gain			
<i>r</i>	0.476**	0.007	0.030
<i>P</i> (two-tailed)	0.001	0.962	0.922
<i>N</i>	48	49	13
OT gain			
<i>r</i>	0.181	0.015	-0.242
<i>P</i> (two-tailed)	0.240	0.926	0.473
<i>N</i>	44	44	11
PT gain			
<i>r</i>	0.243	0.098	-0.313
<i>P</i> (two-tailed)	0.100	0.506	0.298
<i>N</i>	47	48	13
ST gain			
<i>r</i>	0.500	0.463	-0.445
<i>P</i> (two-tailed)	0.098	0.130	0.317
<i>N</i>	12	12	7

* Correlation is significant at 0.05 level (two-tailed).

** Correlation is significant at 0.01 level (two-tailed).

Table 2. Multiple linear regression analysis with forward stepwise entry of independent variables (performed to predict: a) the change in motor/cognitive function and, b) the efficiency of therapies)

Independent variables	Motor function		Cognitive function	
	Discharge	Efficiency	Discharge	Efficiency
Admission motor level	0.23	0.05	0.51***	-0.19
Admission cognitive level	-0.23	0.01	-0.15	0.19
Age (yrs)	-0.41***	-0.28*	-0.01	-0.05
Length of stay (Log)	-0.24*	-0.18	-0.25*	-0.06
Onset-admission interval (Log)	-0.22	-0.11	-0.25*	-0.25*
Co-morbidities	-0.03	0.04	0.07	0.14
Any speech therapy (Y/N)	-0.03	-0.01	-0.51***	0.38**
Occupational therapy intensity	0.03	0.02	-0.04	0.35**
Physical therapy intensity	-0.38**	0.26*	-0.07	-0.18

Degrees of freedom: 9.38; R^2 : motor discharge, 0.57***, motor efficiency 0.19, cognitive discharge 0.48***, cognitive efficiency 0.34*

* Correlation is significant at the 0.05 level (one-tailed).

** Correlation is significant at the 0.01 level (one-tailed).

*** Correlation is significant at < 0.01 level (one-tailed).

significant. Therapy intensity was not associated with reduction of impairment.

• *Activity level improves significantly from admission to discharge*

Multivariate analysis of variance was used to describe improvement in physical and occupational therapy-measured function from admission to discharge. PT-measured function improved from admission ($x = 31.0$) to discharge (62.6), as did OT-measured function ($x = 41.8, 73.9$). While PT function was lower than OT function at both time points, the gains were equivalent. Changes in speech function were not evaluated because the number of patients receiving speech services was relatively small.

- *Increased activity is positively correlated with therapeutic interventions*
Pearson correlation coefficients were used to describe the association between intensities of OT, PT and ST with improvement in generic and discipline-specific measures of activity. Table 1 shows that intensity of OT was correlated with motor and cognitive gains such that greater intensity of OT was associated with greater motor and cognitive gains. Intensity of PT and ST was not significantly correlated with any measure of gain.

- *Greater motor and cognitive function at discharge is achieved by patients who are younger, have higher admission motor and cognitive measures, longer lengths of stay (the period between onset of stroke and admission to the rehabilitation hospital), receive speech therapy, and receive more intense occupational and physical therapy.*

Multiple linear regressions with forward stepwise entry of independent variables were used to predict discharge motor function using age, length of stay, onset-admission interval, admission motor and cognitive measures, receipt of any speech therapy, and intensity of OT and PT [Table 2]. Sixty-four percent of the adjusted variance in discharge motor function was explained by four variables: age, admission motor function, admission cognitive function, and receipt of any speech therapy. Younger patients, those admitted with *higher* motor function, *higher* cognitive function, and who received *any* speech therapy tended to be discharged at a *higher* motor level.

Eighty-one percent of the adjusted variance in cognitive function at discharge was explained by three variables: cognitive function at admission, the period between onset of stroke and admission to the rehabilitation hospital, and OT intensity. Patients who were admitted with *higher* cognitive function had been admitted earlier to a rehabilitation hospital, and who received *more intense* occupational therapy tended to be discharged at a *higher* cognitive level.

Discussion

A significant reduction in impairment from admission to discharge, and an improvement in motor and cognitive components of the FIM as well as in physical and occupational therapy-measured activity level were demonstrated in this study, thus replicating the findings of others [9]. These results highlight several issues regarding the provision of treatment and have potential implications for rehabilitation outcome. Therapy intensity was not related to reduction in level of impairment. Activity and impairment levels were correlated both at admission and at discharge.

Treatment effects may depend not only on the "total dose" of therapy provided, but also on when and how an intervention is scheduled. In this sample, treatment was begun after an initial multidisciplinary assessment. The usual treatment consists of daily sessions, 5 days a week, for every therapeutic modality deemed necessary. The patient is reassessed every 2 to 3 weeks and changes in the treatment plan are introduced accordingly.

Goeland's [10] demonstration of stages of motor impairment recovery suggests that the effects of therapy may vary during early to late periods of recovery. Most functional recovery occurs within the first 3 months after onset of stroke [11]. The timing of therapy has two considerations: when it is provided, and the way

it is provided. For example, one hour of treatment can be given once a day or it might be divided into three sessions – morning, noon and evening. The nature of motor learning can depend on how training is provided. In normal subjects, learning skilled motor performance is acquired in several stages. This time course might reflect basic mechanisms of neural plasticity in the adult brain [12]. The extent to which the motor learning process in normal subjects is analogous to the recovery process of patients following brain damage who are receiving motor training therapy is not clear. The work of Karni and associates [13] is relevant; these investigators used functional MRI and demonstrated a slowly evolving, long-term process of reorganization of the adult motor cortex that might underline the acquisition and retention of motor skills.

While early referral to rehabilitation is associated with better functional outcomes [14], it is still too early to provide clear recommendations regarding when to initiate rehabilitation, how much therapy to provide, and what kind of therapy results in optimal outcomes. Delays in admission to rehabilitation may reflect both patients' readiness for rehabilitation and administrative inefficiencies. Not documented here was the date when patients were ready to transfer; thus, we cannot distinguish whether the timing of the patient's transfer to the rehabilitation hospital was the consequence of his/her "readiness" or due to administrative reasons.

Influence of therapy on impairment and disability reduction

Increased activity was positively correlated with one therapeutic intervention – occupational therapy. The intensity of OT was correlated with motor and cognitive gains such that greater intensity of OT was associated with greater motor and cognitive improvements. Intensity of PT and ST was not significantly correlated with any measure of gain. It was important to distinguish between generic and discipline-specific measures of activity in evaluating treatment effects. Only a few studies have directly addressed the influence of therapy on impairment and disability reduction. Langhorne et al. [15] dealt with questions concerning physical therapy treatment and found that more intensive physical therapy may be associated with enhanced rate of recovery, however their conclusions are not definitive. It is difficult to demonstrate the efficacy of specific physical modalities in specific impairments such as low back pain [16].

Sunderland and co-workers [17] conducted a single-blind, randomized study of 132 stroke patients to examine whether increased physical therapy would lead to better recovery following hemiplegia. The patients were assigned to traditional therapy (based on the "Bobath" theory where active movement is not encouraged until abnormal muscle tone is well controlled) or enhanced therapy (emphasis on setting the patient tasks of graded difficulty and providing objective feedback on performance). Better gains in recovery due to enhanced physical therapy were observed. At 6 months after stroke the enhanced therapy group showed a small but statistically significant advantage in recovery of strength and range and speed of movement. These gains were apparent on tests of strength and range of movement, and on a test of manual dexterity for the more able patients.

Controversy regarding the benefits of focused rehabilitation began in the late 1980s when two opposing opinions were expressed by neurologists. Reding and McDowell [18] stressed the importance of therapy since it allows patients to cope with residual deficits more effectively, thus enabling greater independence; Dobkin [19] argued the reverse. Brodie et al. [20] argued that occupational therapy could enhance activity. In a similar population, Spivack et al. [21] investigated the effects of treatment intensity on rehabilitation outcomes in traumatic brain injury patients. Intensity of treatment was measured according to the total hours of treatment that were provided during a day or a month. The authors concluded that intense treatment over an extended period might enable patients to achieve earlier rehabilitation gains. The rehabilitation intervention may have an effect of improving function that cannot be attributed to neurologic recovery [8].

More recently, Levy and colleagues [22] demonstrated that in chronic upper-limb stroke hemiparesis, constraint-induced movement therapy can produce significant functional improvement and its ability to affect plasticity as demonstrated by studies of functional MRI. Treatment consisted of 6 hours of daily upper limb training for 2 weeks.

Still, there are no clear criteria for the appropriate use of rehabilitation resources in such patients. Due to a lack of consensus on the definition of efficiency and intensity, cost-effectiveness cannot be calculated. We suggest that evaluating the effect of intervention should clearly differentiate between care and therapy. Care includes management and prevention of general deterioration, while therapy includes specific modalities aimed at specific goals such as stimulation of the recovery processes, improvement of motor control, recovery of communicative skills, and improvement of mood and psychological well being.

Wade and De Jong [23] in a recent review concluded that there is no current evidence to identify a minimum or maximum effective intervention. A clear-cut recommendation about "low band" patients was that they would achieve only limited functional gains during rehabilitation, regardless of the therapy provided. Clearly, policies on admission criteria involve ethical as well as financial issues. Alexander [24] pointed out the lack of a published algorithm to provide adequate guidance regarding the proper level of rehabilitation services in any particular setting. A variety of difficult-to-document factors affect outcomes, such as the patient's living environment, family support, social and cultural background, and emotional status.

Limitations of the study include a relatively small sample and inclusion of patients from only one facility. The small sample limits statistical power to detect potentially important relationships. However, the patients were referred from throughout Israel and represent diverse cultural backgrounds. Co-linearity among the predictors, specifically motor and cognitive functional status at admission, limits the extent to which the effects of predictors can be interpreted unambiguously. Curvilinear relationships between functional status at admission and discharge functional status and gains do not appear to be an issue. The quadratic and cubic relationships were essentially the same as the linear relationships.

Conclusions

This study examined the link between "management" and "gains" during the period of inpatient rehabilitation treatment for stroke patients. We looked at the relationships between the amount and type of therapy during the inpatient rehabilitation period. Our sample was relatively small and heterogeneous in terms of the patients' functional abilities. Consequently, our results cannot be generalized to the whole population of stroke patients. Further efforts to identify the best timing, modalities, intensity and frequency of the different possible treatments would improve the cost/benefit equation of stroke patients' rehabilitation. Such studies would have a potential impact on clinical care decisions for patients undergoing post-stroke rehabilitation, with the general aim of enhancing the effectiveness of rehabilitation [25].

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Capsule

New approach for enhancing vaccine potency

Vaccines are designed to generate robust immunity through the co-activation of the adaptive and innate arms of the immune system. This is achieved by steering responses to antigenic epitopes by helper T (TH) cells, antigen-presenting dendritic cells (DCs), and antibody-producing B cells or the cytotoxic lymphocytes (CTLs) that ultimately execute pathogen clearance. However, the poor inherent immunogenicity of peptide epitopes favored in some vaccine formulas dictates the need for including complex and potentially toxic adjuvants that stimulate the essential priming activity of DCs. Jackson and associates have refined this approach by synthesizing structures containing TH epitopes coupled to B cell or CTL target epitopes. These were

linked via a lipid moiety, which served to activate DCs through binding and activation of the innate signaling receptor TLR2. With different epitope combinations, strong antibody and CTL responses could be elicited in models of viral and bacterial infection, as well as to tumors, and were comparable to responses to an adjuvant traditionally used in vaccines. The ability to combine adjuvant and antigenic properties in a single synthetic formula offers an attractive approach for future vaccine design.

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E. Israeli

Capsule

Curing cancer with anaerobic bullets

The spore-forming *Clostridium* species of bacteria are notorious for the toxins they can generate, including botulinum and tetanus. They also prefer to live where there is little oxygen. Starting with early observations by William Coley in the 19th century of cancer remission in some patients surviving post-operative infection, Agrawal and collaborators used these two characteristics of *Clostridium novyi*-NT for experimental cancer therapy. They injected mice bearing large established tumors with spores of an attenuated strain of the bacterium and showed that the spores exclusively germinated within the hypoxic cores of the tumors and destroyed all but the peripheral oxygenated

cells. These cells subsequently continued to expand, but about 30% of the mice were cured of the cancer in the absence of radio- or chemotherapy. This happened because a potent immune response to the cancer cells was generated, such that all the cured mice subsequently rejected transplanted tumor cells of the same type and kept the bacteria under control. Similar success was observed in rabbits and rats, but it is unknown whether humans would generate similarly effective immune responses.

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