



See a Social Security Number? Say Something!
Report Privacy Problems to <https://public.resource.org/privacy>
Or call the IRS Identity Theft Hotline at 1-800-908-4490



Return of Private Foundation
 or Section 4947(a)(1) Nonexempt Charitable Trust
 Treated as a Private Foundation

2009

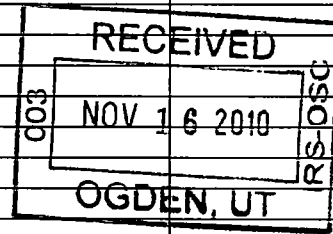
Note: The foundation may be able to use a copy of this return to satisfy state reporting requirements

For calendar year 2009, or tax year beginning , 2009, and ending , 20

G Check all that apply. Initial return Initial return of a former public charity Final return
 Amended return Address change Name change

Use the IRS label. Otherwise, print or type. See Specific Instructions.	Name of foundation THE NOTSEW ORM SANDS FOUNDATION		A Employer identification number 76-0455176
	Number and street (or P O box number if mail is not delivered to street address) 2470 S. DAIRY ASHFORD	Room/suite 802	B Telephone number (see page 10 of the instructions) (281) 497-0744
	City or town, state, and ZIP code HOUSTON, TX 77077		C If exemption application is pending, check here <input type="checkbox"/>
			D 1 Foreign organizations, check here <input type="checkbox"/> 2. Foreign organizations meeting the 85% test, check here and attach computation <input type="checkbox"/>
H Check type of organization <input checked="" type="checkbox"/> Section 501(c)(3) exempt private foundation <input type="checkbox"/> Section 4947(a)(1) nonexempt charitable trust <input type="checkbox"/> Other taxable private foundation			E If private foundation status was terminated under section 507(b)(1)(A), check here <input type="checkbox"/>
I Fair market value of all assets at end of year (from Part II, col (c), line 16) \$ 13,183.		J Accounting method <input checked="" type="checkbox"/> Cash <input type="checkbox"/> Accrual <input type="checkbox"/> Other (specify) _____ (Part I, column (d) must be on cash basis)	F If the foundation is in a 60-month termination under section 507(b)(1)(B), check here <input type="checkbox"/>

Part I Analysis of Revenue and Expenses (The total of amounts in columns (b), (c), and (d) may not necessarily equal the amounts in column (a) (see page 11 of the instructions))		(a) Revenue and expenses per books	(b) Net investment income	(c) Adjusted net income	(d) Disbursements for charitable purposes (cash basis only)
Revenue	1 Contributions, gifts, grants, etc., received (attach schedule) <input type="checkbox"/> if the foundation is not required to attach Sch. B.	936,718.			
	2 Check <input type="checkbox"/>				
	3 Interest on savings and temporary cash investments	8.	8.		ATCH 1
	4 Dividends and interest from securities				
	5a Gross rents				
	b Net rental income or (loss)				
	6a Net gain or (loss) from sale of assets not on line 10				
	b Gross sales price for all assets on line 6a				
	7 Capital gain net income (from Part IV, line 2)				
	8 Net short-term capital gain				
	9 Income modifications				
	10 a Gross sales less returns and allowances				
b Less Cost of goods sold					
c Gross profit or (loss) (attach schedule)					
11 Other income (attach schedule)					
12 Total. Add lines 1 through 11	936,726.	8.			
Operating and Administrative Expenses	13 Compensation of officers, directors, trustees, etc.	5,000.	1,667.		3,333.
	14 Other employee salaries and wages				
	15 Pension plans, employee benefits				
	16a Legal fees (attach schedule) ATCH 2	205.	0.	0.	205.
	b Accounting fees (attach schedule) ATCH 3	13,313.	9,319.	0.	3,994.
	c Other professional fees (attach schedule)				
	17 Interest				
	18 Taxes (attach schedule) (see page 14 of the instructions) **	15.	5.		10.
	19 Depreciation (attach schedule) and depletion				
	20 Occupancy				
	21 Travel, conferences, and meetings				
	22 Printing and publications				
	23 Other expenses (attach schedule) ATCH 5	90.			90.
	24 Total operating and administrative expenses. Add lines 13 through 23	18,623.	10,991.	0.	7,632.
	25 Contributions, gifts, grants paid	929,258.			929,258.
26 Total expenses and disbursements. Add lines 24 and 25	947,881.	10,991.	0.	936,890.	
27 Subtract line 26 from line 12					
a Excess of revenue over expenses and disbursements	-11,155.				
b Net investment income (if negative, enter -0-)		-0-			
c Adjusted net income (if negative, enter -0-)			-0-		



SCANNED NOV 19 2010

Part II Balance Sheets		Attached schedules and amounts in the description column should be for end-of-year amounts only (See instructions)			
		Beginning of year (a) Book Value	End of year (b) Book Value (c) Fair Market Value		
Assets	1	Cash - non-interest-bearing	11,728.	656.	656.
	2	Savings and temporary cash investments	10,001.	9,918.	9,918.
	3	Accounts receivable 600.			
		Less allowance for doubtful accounts	600.	600.	600.
	4	Pledges receivable			
		Less allowance for doubtful accounts			
	5	Grants receivable			
	6	Receivables due from officers, directors, trustees, and other disqualified persons (attach schedule) (see page 16 of the instructions)			
	7	Other notes and loans receivable (attach schedule)			
		Less allowance for doubtful accounts			
	8	Inventories for sale or use			
	9	Prepaid expenses and deferred charges	2,009.	2,009.	2,009.
	10 a	Investments - U S and state government obligations (attach schedule)			
	b	Investments - corporate stock (attach schedule)			
	c	Investments - corporate bonds (attach schedule)			
	11	Investments - land, buildings, and equipment basis Less accumulated depreciation (attach schedule)			
12	Investments - mortgage loans				
13	Investments - other (attach schedule)				
14	Land, buildings, and equipment basis Less accumulated depreciation (attach schedule)				
15	Other assets (describe)				
16	Total assets (to be completed by all filers - see the instructions Also, see page 1, item I)	24,338.	13,183.	13,183.	
Liabilities	17	Accounts payable and accrued expenses			
	18	Grants payable			
	19	Deferred revenue			
	20	Loans from officers, directors, trustees, and other disqualified persons			
	21	Mortgages and other notes payable (attach schedule)			
	22	Other liabilities (describe <u>ATCH 6</u>)	400.	400.	
23	Total liabilities (add lines 17 through 22)	400.	400.		
Net Assets or Fund Balances	Foundations that follow SFAS 117, check here <input checked="" type="checkbox"/>				
	and complete lines 24 through 26 and lines 30 and 31.				
	24	Unrestricted	23,938.	12,783.	
	25	Temporarily restricted			
	26	Permanently restricted			
	Foundations that do not follow SFAS 117, check here and complete lines 27 through 31. <input type="checkbox"/>				
	27	Capital stock, trust principal, or current funds			
	28	Paid-in or capital surplus, or land, bldg, and equipment fund			
29	Retained earnings, accumulated income, endowment, or other funds				
30	Total net assets or fund balances (see page 17 of the instructions)	23,938.	12,783.		
31	Total liabilities and net assets/fund balances (see page 17 of the instructions)	24,338.	13,183.		

Part III Analysis of Changes in Net Assets or Fund Balances		
1	Total net assets or fund balances at beginning of year - Part II, column (a), line 30 (must agree with end-of-year figure reported on prior year's return)	23,938.
2	Enter amount from Part I, line 27a	-11,155.
3	Other increases not included in line 2 (itemize)	
4	Add lines 1, 2, and 3	12,783.
5	Decreases not included in line 2 (itemize)	
6	Total net assets or fund balances at end of year (line 4 minus line 5) - Part II, column (b), line 30	12,783.

Part IV Capital Gains and Losses for Tax on Investment Income

(a) List and describe the kind(s) of property sold (e.g., real estate, 2-story brick warehouse, or common stock, 200 shs MLC Co)		(b) How acquired P-Purchase D-Donation	(c) Date acquired (mo, day, yr)	(d) Date sold (mo, day, yr)
1a				
b				
c				
d				
e				
(e) Gross sales price	(f) Depreciation allowed (or allowable)	(g) Cost or other basis plus expense of sale	(h) Gain or (loss) (e) plus (f) minus (g)	
a				
b				
c				
d				
e				
Complete only for assets showing gain in column (h) and owned by the foundation on 12/31/69			(i) Gains (Col (h) gain minus col (k), but not less than -0-) or Losses (from col (h))	
(i) F M V as of 12/31/69	(j) Adjusted basis as of 12/31/69	(k) Excess of col (i) over col (j), if any		
a				
b				
c				
d				
e				
2 Capital gain net income or (net capital loss)	{ If gain, also enter in Part I, line 7 If (loss), enter -0- in Part I, line 7 }		2	
3 Net short-term capital gain or (loss) as defined in sections 1222(5) and (6) If gain, also enter in Part I, line 8, column (c) (see pages 13 and 17 of the instructions) If (loss), enter -0- in Part I, line 8	{ }		3	

Part V Qualification Under Section 4940(e) for Reduced Tax on Net Investment Income

(For optional use by domestic private foundations subject to the section 4940(a) tax on net investment income)

If section 4940(d)(2) applies, leave this part blank

Was the foundation liable for the section 4942 tax on the distributable amount of any year in the base period? Yes No
 If "Yes," the foundation does not qualify under section 4940(e) Do not complete this part

1 Enter the appropriate amount in each column for each year, see page 18 of the instructions before making any entries

(a) Base period years Calendar year (or tax year beginning in)	(b) Adjusted qualifying distributions	(c) Net value of noncharitable-use assets	(d) Distribution ratio (col (b) divided by col (c))
2008	3,118,071.	336,374.	9.269655
2007	1,898,300.	171,380.	11.076555
2006	447,942.	394,848.	1.134467
2005	1,514,714.	1,039,378.	1.457327
2004	648,627.	2,201,879.	0.294579
2 Total of line 1, column (d)			23.232583
3 Average distribution ratio for the 5-year base period - divide the total on line 2 by 5, or by the number of years the foundation has been in existence if less than 5 years			4.646517
4 Enter the net value of noncharitable-use assets for 2009 from Part X, line 5			11,585.
5 Multiply line 4 by line 3			53,830.
6 Enter 1% of net investment income (1% of Part I, line 27b)			
7 Add lines 5 and 6			53,830.
8 Enter qualifying distributions from Part XII, line 4 If line 8 is equal to or greater than line 7, check the box in Part VI, line 1b, and complete that part using a 1% tax rate See the Part VI instructions on page 18			936,890.

Part VI Excise Tax Based on Investment Income (Section 4940(a), 4940(b), 4940(e), or 4948 - see page 18 of the instructions)

1a	Exempt operating foundations described in section 4940(d)(2), check here <input type="checkbox"/> and enter "N/A" on line 1 Date of ruling or determination letter _____ (attach copy of ruling letter if necessary - see instructions)		
b	Domestic foundations that meet the section 4940(e) requirements in Part V, check here <input checked="" type="checkbox"/> and enter 1% of Part I, line 27b	1	0.
c	All other domestic foundations enter 2% of line 27b Exempt foreign organizations enter 4% of Part I, line 12, col (b)		
2	Tax under section 511 (domestic section 4947(a)(1) trusts and taxable foundations only Others enter -0-)	2	
3	Add lines 1 and 2	3	0.
4	Subtitle A (income) tax (domestic section 4947(a)(1) trusts and taxable foundations only Others enter -0-)	4	0.
5	Tax based on investment income. Subtract line 4 from line 3. If zero or less, enter -0-	5	0.
6	Credits/Payments		
a	2009 estimated tax payments and 2008 overpayment credited to 2009	6a	2,009.
b	Exempt foreign organizations-tax withheld at source	6b	0.
c	Tax paid with application for extension of time to file (Form 8868)	6c	0.
d	Backup withholding erroneously withheld	6d	
7	Total credits and payments Add lines 6a through 6d	7	2,009.
8	Enter any penalty for underpayment of estimated tax Check here <input type="checkbox"/> if Form 2220 is attached	8	
9	Tax due. If the total of lines 5 and 8 is more than line 7, enter amount owed	9	
10	Overpayment. If line 7 is more than the total of lines 5 and 8, enter the amount overpaid	10	2,009.
11	Enter the amount of line 10 to be Credited to 2010 estimated tax 2,009. Refunded	11	

Part VII-A Statements Regarding Activities

	Yes	No
1a During the tax year, did the foundation attempt to influence any national, state, or local legislation or did it participate or intervene in any political campaign?		X
1b Did it spend more than \$100 during the year (either directly or indirectly) for political purposes (see page 19 of the instructions for definition)? If the answer is "Yes" to 1a or 1b, attach a detailed description of the activities and copies of any materials published or distributed by the foundation in connection with the activities		X
1c Did the foundation file Form 1120-POL for this year?		X
2 Enter the amount (if any) of tax on political expenditures (section 4955) imposed during the year (1) On the foundation \$ _____ (2) On foundation managers \$ _____		
e Enter the reimbursement (if any) paid by the foundation during the year for political expenditure tax imposed on foundation managers \$ _____		
2 Has the foundation engaged in any activities that have not previously been reported to the IRS? If "Yes," attach a detailed description of the activities		X
3 Has the foundation made any changes, not previously reported to the IRS, in its governing instrument, articles of incorporation, or bylaws, or other similar instruments? If "Yes," attach a conformed copy of the changes		X
4a Did the foundation have unrelated business gross income of \$1,000 or more during the year?		X
4b If "Yes," has it filed a tax return on Form 990-T for this year?		
5 Was there a liquidation, termination, dissolution, or substantial contraction during the year? If "Yes," attach the statement required by General Instruction T		X
6 Are the requirements of section 508(e) (relating to sections 4941 through 4945) satisfied either • By language in the governing instrument, or • By state legislation that effectively amends the governing instrument so that no mandatory directions that conflict with the state law remain in the governing instrument?	X	
7 Did the foundation have at least \$5,000 in assets at any time during the year? If "Yes," complete Part II, col (c), and Part XV	X	
8a Enter the states to which the foundation reports or with which it is registered (see page 19 of the instructions) TX,		
b If the answer is "Yes" to line 7, has the foundation furnished a copy of Form 990-PF to the Attorney General (or designate) of each state as required by General Instruction G? If "No," attach explanation	X	
9 Is the foundation claiming status as a private operating foundation within the meaning of section 4942(j)(3) or 4942(j)(5) for calendar year 2009 or the taxable year beginning in 2009 (see instructions for Part XIV on page 27)? If "Yes," complete Part XIV		X
10 Did any persons become substantial contributors during the tax year? If "Yes," attach a schedule listing their names and addresses		X

Part VII-A Statements Regarding Activities (continued)

11 At any time during the year, did the foundation, directly or indirectly, own a controlled entity within the meaning of section 512(b)(13)? If "Yes," attach schedule (see page 20 of the instructions) 11 X
12 Did the foundation acquire a direct or indirect interest in any applicable insurance contract before August 17, 2008? 12 X
13 Did the foundation comply with the public inspection requirements for its annual returns and exemption application? 13 X
Website address N/A
14 The books are in care of CONNIE MCCLURE Telephone no 416-967-7841
Located at ATTACHMENT 7 ZIP + 4 M4T 2S3
15 Section 4947(a)(1) nonexempt charitable trusts filing Form 990-PF in lieu of Form 1041 - Check here and enter the amount of tax-exempt interest received or accrued during the year 15

Part VII-B Statements Regarding Activities for Which Form 4720 May Be Required

File Form 4720 if any item is checked in the "Yes" column, unless an exception applies.

1a During the year did the foundation (either directly or indirectly)
(1) Engage in the sale or exchange, or leasing of property with a disqualified person? Yes No
(2) Borrow money from, lend money to, or otherwise extend credit to (or accept it from) a disqualified person? Yes No
(3) Furnish goods, services, or facilities to (or accept them from) a disqualified person? Yes No
(4) Pay compensation to, or pay or reimburse the expenses of, a disqualified person? Yes No
(5) Transfer any income or assets to a disqualified person (or make any of either available for the benefit or use of a disqualified person)? Yes No
(6) Agree to pay money or property to a government official? (Exception. Check "No" if the foundation agreed to make a grant to or to employ the official for a period after termination of government service, if terminating within 90 days) Yes No
b If any answer is "Yes" to 1a(1)-(6), did any of the acts fail to qualify under the exceptions described in Regulations section 53.4941(d)-3 or in a current notice regarding disaster assistance (see page 20 of the instructions)? 1b X
Organizations relying on a current notice regarding disaster assistance check here
c Did the foundation engage in a prior year in any of the acts described in 1a, other than excepted acts, that were not corrected before the first day of the tax year beginning in 2009? 1c X
2 Taxes on failure to distribute income (section 4942) (does not apply for years the foundation was a private operating foundation defined in section 4942(j)(3) or 4942(j)(5))
a At the end of tax year 2009, did the foundation have any undistributed income (lines 6d and 6e, Part XIII) for tax year(s) beginning before 2009? Yes No
If "Yes," list the years
b Are there any years listed in 2a for which the foundation is not applying the provisions of section 4942(a)(2) (relating to incorrect valuation of assets) to the year's undistributed income? (If applying section 4942(a)(2) to all years listed, answer "No" and attach statement - see page 20 of the instructions) 2b
c If the provisions of section 4942(a)(2) are being applied to any of the years listed in 2a, list the years here
3a Did the foundation hold more than a 2% direct or indirect interest in any business enterprise at any time during the year? Yes No
b If "Yes," did it have excess business holdings in 2009 as a result of (1) any purchase by the foundation or disqualified persons after May 26, 1969, (2) the lapse of the 5-year period (or longer period approved by the Commissioner under section 4943(c)(7)) to dispose of holdings acquired by gift or bequest, or (3) the lapse of the 10-, 15-, or 20-year first phase holding period? (Use Schedule C, Form 4720, to determine if the foundation had excess business holdings in 2009) 3b
4a Did the foundation invest during the year any amount in a manner that would jeopardize its charitable purposes? 4a X
b Did the foundation make any investment in a prior year (but after December 31, 1969) that could jeopardize its charitable purpose that had not been removed from jeopardy before the first day of the tax year beginning in 2009? 4b X

Part VII-B Statements Regarding Activities for Which Form 4720 May Be Required (continued)

5a During the year did the foundation pay or incur any amount to

(1) Carry on propaganda, or otherwise attempt to influence legislation (section 4945(e))? Yes No

(2) Influence the outcome of any specific public election (see section 4955), or to carry on, directly or indirectly, any voter registration drive? Yes No

(3) Provide a grant to an individual for travel, study, or other similar purposes? Yes No

(4) Provide a grant to an organization other than a charitable, etc., organization described in section 509(a)(1), (2), or (3), or section 4940(d)(2)? (see page 22 of the instructions) Yes No

(5) Provide for any purpose other than religious, charitable, scientific, literary, or educational purposes, or for the prevention of cruelty to children or animals? Yes No

b If any answer is "Yes" to 5a(1)-(5), did any of the transactions fail to qualify under the exceptions described in Regulations section 53.4945 or in a current notice regarding disaster assistance (see page 22 of the instructions)? Yes No
 Organizations relying on a current notice regarding disaster assistance check here

c If the answer is "Yes" to question 5a(4), does the foundation claim exemption from the tax because it maintained expenditure responsibility for the grant? ATTACHMENT 8 Yes No
 If "Yes," attach the statement required by Regulations section 53.4945-5(d)

6a Did the foundation, during the year, receive any funds, directly or indirectly, to pay premiums on a personal benefit contract? Yes No

b Did the foundation, during the year, pay premiums, directly or indirectly, on a personal benefit contract? Yes No
 If "Yes" to 6b, file Form 8870

7a At any time during the tax year, was the foundation a party to a prohibited tax shelter transaction? Yes No

b If yes, did the foundation receive any proceeds or have any net income attributable to the transaction? Yes No

Part VIII Information About Officers, Directors, Trustees, Foundation Managers, Highly Paid Employees, and Contractors

1 List all officers, directors, trustees, foundation managers and their compensation (see page 22 of the instructions).

(a) Name and address	(b) Title, and average hours per week devoted to position	(c) Compensation (if not paid, enter -0-)	(d) Contributions to employee benefit plans and deferred compensation	(e) Expense account, other allowances
ATTACHMENT 9		5,000.	-0-	-0-

2 Compensation of five highest-paid employees (other than those included on line 1 - see page 23 of the instructions). If none, enter "NONE."

(a) Name and address of each employee paid more than \$50,000	(b) Title, and average hours per week devoted to position	(c) Compensation	(d) Contributions to employee benefit plans and deferred compensation	(e) Expense account, other allowances
NONE				

Total number of other employees paid over \$50,000

Part VIII Information About Officers, Directors, Trustees, Foundation Managers, Highly Paid Employees, and Contractors (continued)

3 Five highest-paid independent contractors for professional services (see page 23 of the instructions). If none, enter "NONE."

(a) Name and address of each person paid more than \$50,000	(b) Type of service	(c) Compensation
NONE		

Total number of others receiving over \$50,000 for professional services NONE

Part IX-A Summary of Direct Charitable Activities

List the foundation's four largest direct charitable activities during the tax year. Include relevant statistical information such as the number of organizations and other beneficiaries served, conferences convened, research papers produced, etc.	Expenses
1 N/A	
2	
3	
4	

Part IX-B Summary of Program-Related Investments (see page 23 of the instructions)

Describe the two largest program-related investments made by the foundation during the tax year on lines 1 and 2	Amount
1 NONE	
2	
All other program-related investments See page 24 of the instructions	
3 NONE	
Total. Add lines 1 through 3	

Part X Minimum Investment Return (All domestic foundations must complete this part. Foreign foundations, see page 24 of the instructions.)

1	Fair market value of assets not used (or held for use) directly in carrying out charitable, etc., purposes		
a	Average monthly fair market value of securities	1a	
b	Average of monthly cash balances	1b	11,761.
c	Fair market value of all other assets (see page 24 of the instructions)	1c	0.
d	Total (add lines 1a, b, and c)	1d	11,761.
e	Reduction claimed for blockage or other factors reported on lines 1a and 1c (attach detailed explanation)	1e	
2	Acquisition indebtedness applicable to line 1 assets	2	0.
3	Subtract line 2 from line 1d	3	11,761.
4	Cash deemed held for charitable activities. Enter 1 1/2 % of line 3 (for greater amount, see page 25 of the instructions)	4	176.
5	Net value of noncharitable-use assets. Subtract line 4 from line 3. Enter here and on Part V, line 4	5	11,585.
6	Minimum investment return. Enter 5% of line 5	6	579.

Part XI Distributable Amount (see page 25 of the instructions) (Section 4942(j)(3) and (j)(5) private operating foundations and certain foreign organizations check here and do not complete this part)

1	Minimum investment return from Part X, line 6	1	579.
2a	Tax on investment income for 2009 from Part VI, line 5	2a	0.
b	Income tax for 2009 (This does not include the tax from Part VI)	2b	
c	Add lines 2a and 2b	2c	0.
3	Distributable amount before adjustments. Subtract line 2c from line 1	3	579.
4	Recoveries of amounts treated as qualifying distributions	4	
5	Add lines 3 and 4	5	579.
6	Deduction from distributable amount (see page 25 of the instructions)	6	
7	Distributable amount as adjusted. Subtract line 6 from line 5. Enter here and on Part XIII, line 1	7	579.

Part XII Qualifying Distributions(see page 25 of the instructions)

1	Amounts paid (including administrative expenses) to accomplish charitable, etc., purposes		
a	Expenses, contributions, gifts, etc. - total from Part I, column (d), line 26	1a	936,890.
b	Program-related investments - total from Part IX-B	1b	0.
2	Amounts paid to acquire assets used (or held for use) directly in carrying out charitable, etc., purposes	2	0.
3	Amounts set aside for specific charitable projects that satisfy the		
a	Suitability test (prior IRS approval required)	3a	0.
b	Cash distribution test (attach the required schedule)	3b	0.
4	Qualifying distributions. Add lines 1a through 3b. Enter here and on Part V, line 8, and Part XIII, line 4	4	936,890.
5	Foundations that qualify under section 4940(e) for the reduced rate of tax on net investment income. Enter 1% of Part I, line 27b (see page 26 of the instructions)	5	
6	Adjusted qualifying distributions. Subtract line 5 from line 4	6	936,890.

Note: The amount on line 6 will be used in Part V, column (b), in subsequent years when calculating whether the foundation qualifies for the section 4940(e) reduction of tax in those years

Part XIII Undistributed Income (see page 26 of the instructions)

	(a) Corpus	(b) Years prior to 2008	(c) 2008	(d) 2009
1 Distributable amount for 2009 from Part XI, line 7				579.
2 Undistributed income, if any, as of the end of 2009				
a Enter amount for 2008 only				
b Total for prior years 20 07, 20 06, 20 05				
3 Excess distributions carryover, if any, to 2009				
a From 2004	548,821.			
b From 2005	1,471,545.			
c From 2006	429,002.			
d From 2007	1,890,045.			
e From 2008	3,101,252.			
f Total of lines 3a through e	7,440,665.			
4 Qualifying distributions for 2009 from Part XII, line 4 ▶ \$	936,890.			
a Applied to 2008, but not more than line 2a				
b Applied to undistributed income of prior years (Election required - see page 26 of the instructions)				
c Treated as distributions out of corpus (Election required - see page 26 of the instructions)				
d Applied to 2009 distributable amount				579.
e Remaining amount distributed out of corpus	936,311.			
5 Excess distributions carryover applied to 2009 (If an amount appears in column (d), the same amount must be shown in column (a))				
6 Enter the net total of each column as indicated below:	8,376,976.			
a Corpus Add lines 3f, 4c, and 4e Subtract line 5				
b Prior years' undistributed income Subtract line 4b from line 2b				
c Enter the amount of prior years' undistributed income for which a notice of deficiency has been issued, or on which the section 4942(a) tax has been previously assessed.				
d Subtract line 6c from line 6b Taxable amount - see page 27 of the instructions				
e Undistributed income for 2008 Subtract line 4a from line 2a Taxable amount - see page 27 of the instructions				
f Undistributed income for 2009 Subtract lines 4d and 5 from line 1 This amount must be distributed in 2010				
7 Amounts treated as distributions out of corpus to satisfy requirements imposed by section 170(b)(1)(F) or 4942(g)(3) (see page 27 of the instructions)				
8 Excess distributions carryover from 2004 not applied on line 5 or line 7 (see page 27 of the instructions)	548,821.			
9 Excess distributions carryover to 2010. Subtract lines 7 and 8 from line 6a	7,828,155.			
10 Analysis of line 9				
a Excess from 2005	1,471,545.			
b Excess from 2006	429,002.			
c Excess from 2007	1,890,045.			
d Excess from 2008	3,101,252.			
e Excess from 2009	936,311.			

Part XIV Private Operating Foundations (see page 27 of the instructions and Part VII-A, question 9) NOT APPLICABLE

1a If the foundation has received a ruling or determination letter that it is a private operating foundation, and the ruling is effective for 2009, enter the date of the ruling ▶

b Check box to indicate whether the foundation is a private operating foundation described in section 4942(j)(3) or 4942(j)(5)

	Pnor 3 years				(e) Total
	(a) 2009	(b) 2008	(c) 2007	(d) 2006	
2a Enter the lesser of the adjusted net income from Part I or the minimum investment return from Part X for each year listed					
b 85% of line 2a					
c Qualifying distributions from Part XII, line 4 for each year listed					
d Amounts included in line 2c not used directly for active conduct of exempt activities					
e Qualifying distributions made directly for active conduct of exempt activities Subtract line 2d from line 2c					
3 Complete 3a, b, or c for the alternative test relied upon					
a "Assets" alternative test - enter					
(1) Value of all assets					
(2) Value of assets qualifying under section 4942(j)(3)(B)(i)					
b "Endowment" alternative test - enter 2/3 of minimum investment return shown in Part X, line 6 for each year listed					
c "Support" alternative test - enter					
(1) Total support other than gross investment income (interest, dividends, rents, payments on securities loans (section 512(a)(5)), or royalties)					
(2) Support from general public and 5 or more exempt organizations as provided in section 4942(j)(3)(B)(ii)					
(3) Largest amount of support from an exempt organization					
(4) Gross investment income					

Part XV Supplementary Information (Complete this part only if the foundation had \$5,000 or more in assets at any time during the year - see page 28 of the instructions.)

1 Information Regarding Foundation Managers:

a List any managers of the foundation who have contributed more than 2% of the total contributions received by the foundation before the close of any tax year (but only if they have contributed more than \$5,000) (See section 507(d)(2))

CHARLES BURNETT III

b List any managers of the foundation who own 10% or more of the stock of a corporation (or an equally large portion of the ownership of a partnership or other entity) of which the foundation has a 10% or greater interest

NONE

2 Information Regarding Contribution, Grant, Gift, Loan, Scholarship, etc., Programs:

Check here if the foundation only makes contributions to preselected charitable organizations and does not accept unsolicited requests for funds If the foundation makes gifts, grants, etc (see page 28 of the instructions) to individuals or organizations under other conditions, complete items 2a, b, c, and d.

a The name, address, and telephone number of the person to whom applications should be addressed

ATTACHMENT 10

b The form in which applications should be submitted and information and materials they should include

SEE ATTACHMENT 10

c Any submission deadlines

SEE ATTACHMENT 10

d Any restrictions or limitations on awards, such as by geographical areas, charitable fields, kinds of institutions, or other factors

SEE ATTACHMENT 10

Part XV Supplementary Information (continued)

3 Grants and Contributions Paid During the Year or Approved for Future Payment

Recipient Name and address (home or business)	If recipient is an individual, show any relationship to any foundation manager or substantial contributor	Foundation status of recipient	Purpose of grant or contribution	Amount
a <i>Paid during the year</i> ATTACHMENT 11				
Total				▶ 3a 929,258.
b <i>Approved for future payment</i>				
Total				▶ 3b

Part XVII Information Regarding Transfers To and Transactions and Relationships With Noncharitable Exempt Organizations

1 Did the organization directly or indirectly engage in any of the following with any other organization described in section 501(c) of the Code (other than section 501(c)(3) organizations) or in section 527, relating to political organizations?
a Transfers from the reporting foundation to a noncharitable exempt organization of
(1) Cash
(2) Other assets
b Other transactions
(1) Sales of assets to a noncharitable exempt organization
(2) Purchases of assets from a noncharitable exempt organization
(3) Rental of facilities, equipment, or other assets
(4) Reimbursement arrangements
(5) Loans or loan guarantees
(6) Performance of services or membership or fundraising solicitations
c Sharing of facilities, equipment, mailing lists, other assets, or paid employees
d If the answer to any of the above is "Yes," complete the following schedule

Table with 4 columns: (a) Line no, (b) Amount involved, (c) Name of noncharitable exempt organization, (d) Description of transfers, transactions, and sharing arrangements. Row 1 contains 'N/A' for both (b) and (d).

2a Is the foundation directly or indirectly affiliated with, or related to, one or more tax-exempt organizations described in section 501(c) of the Code (other than section 501(c)(3)) or in section 527? Yes No

Table with 3 columns: (a) Name of organization, (b) Type of organization, (c) Description of relationship. All cells are empty.

Under penalties of perjury, I declare that I have examined this return, including accompanying schedules and statements, and to the best of my knowledge and belief, it is true, correct, and complete Declaration of preparer (other than taxpayer or fiduciary) is based on all information of which preparer has any knowledge

Signature of officer or trustee: [Signature], Date: 11/10/10, Title: PRESIDENT. Preparer's signature: [Signature], Date: 11/9/10, Check if self-employed: [], Preparer's identifying number: [], Firm's name: BKD, LLP, 10001 REUNION PLACE, SUITE 400, SAN ANTONIO, TX, EIN: 44-0160260, Phone no: 210.341.9400

Schedule of Contributors

▶ Attach to Form 990, 990-EZ, or 990-PF.

2009

Name of the organization THE NOTSEW ORM SANDS FOUNDATION	Employer identification number 76-0455176
--	---

Organization type (check one)

Filers of:

Section:

Form 990 or 990-EZ

- 501(c)() (enter number) organization
- 4947(a)(1) nonexempt charitable trust not treated as a private foundation
- 527 political organization

Form 990-PF

- 501(c)(3) exempt private foundation
- 4947(a)(1) nonexempt charitable trust treated as a private foundation
- 501(c)(3) taxable private foundation

Check if your organization is covered by the **General Rule** or a **Special Rule**.

Note. Only a section 501(c)(7), (8), or (10) organization can check boxes for both the General Rule and a Special Rule. See instructions.

General Rule

- For an organization filing Form 990, 990-EZ, or 990-PF that received, during the year, \$5,000 or more (in money or property) from any one contributor. Complete Parts I and II.

Special Rules

- For a section 501(c)(3) organization filing Form 990 or 990-EZ that met the 33 1/3 % support test of the regulations under sections 509(a)(1) and 170(b)(1)(A)(vi), and received from any one contributor, during the year, a contribution of the greater of (1) \$5,000 or (2) 2% of the amount on (i) Form 990, Part VIII, line 1h or (ii) Form 990-EZ, line 1. Complete Parts I and II.
- For a section 501(c)(7), (8), or (10) organization filing Form 990 or 990-EZ that received from any one contributor, during the year, aggregate contributions of more than \$1,000 for use *exclusively* for religious, charitable, scientific, literary, or educational purposes, or the prevention of cruelty to children or animals. Complete Parts I, II, and III.
- For a section 501(c)(7), (8), or (10) organization filing Form 990 or 990-EZ that received from any one contributor, during the year, contributions for use *exclusively* for religious, charitable, etc., purposes, but these contributions did not aggregate to more than \$1,000. If this box is checked, enter here the total contributions that were received during the year for an *exclusively* religious, charitable, etc., purpose. Do not complete any of the parts unless the **General Rule** applies to this organization because it received nonexclusively religious, charitable, etc., contributions of \$5,000 or more during the year. ▶ \$ _____

Caution. An organization that is not covered by the General Rule and/or the Special Rules does not file Schedule B (Form 990, 990-EZ, or 990-PF), but it **must** answer "No" on Part IV, line 2 of its Form 990, or check the box on line H of its Form 990-EZ, or on line 2 of its Form 990-PF, to certify that it does not meet the filing requirements of Schedule B (Form 990, 990-EZ, or 990-PF).

Name of organization THE NOTSEW ORM SANDS FOUNDATION

Employer identification number
76-0455176

Part I Contributors (see instructions)

(a) No.	(b) Name, address, and ZIP + 4	(c) Aggregate contributions	(d) Type of contribution
1	CHARLES BURNETT III 1535-E POTOMAC DRIVE HOUSTON, TX 77057-1961	\$ 17,460.	Person <input checked="" type="checkbox"/> Payroll <input type="checkbox"/> Noncash <input type="checkbox"/> (Complete Part II if there is a noncash contribution)
2	THE CHARLES BURNETT BERMUDA SETTLEMENT P.O. BOX 25, REGENCY COURT, GLATEGNY ESP ST. PETER PORT GUERNSEY, GY1 3AP GUERNSEY	\$ 919,258.	Person <input checked="" type="checkbox"/> Payroll <input type="checkbox"/> Noncash <input type="checkbox"/> (Complete Part II if there is a noncash contribution)
		\$ _____	Person <input type="checkbox"/> Payroll <input type="checkbox"/> Noncash <input type="checkbox"/> (Complete Part II if there is a noncash contribution)
		\$ _____	Person <input type="checkbox"/> Payroll <input type="checkbox"/> Noncash <input type="checkbox"/> (Complete Part II if there is a noncash contribution)
		\$ _____	Person <input type="checkbox"/> Payroll <input type="checkbox"/> Noncash <input type="checkbox"/> (Complete Part II if there is a noncash contribution)
		\$ _____	Person <input type="checkbox"/> Payroll <input type="checkbox"/> Noncash <input type="checkbox"/> (Complete Part II if there is a noncash contribution)

ATTACHMENT 1

FORM 990PF, PART I - INTEREST ON TEMPORARY CASH INVESTMENTS

<u>DESCRIPTION</u>	<u>REVENUE AND EXPENSES PER BOOKS</u>	<u>NET INVESTMENT INCOME</u>
BANK OF BUTTERFIELD	8.	8.
TOTAL	<u>8.</u>	<u>8.</u>

ATTACHMENT 2

FORM 990PF, PART I - LEGAL FEES

<u>DESCRIPTION</u>	<u>REVENUE AND EXPENSES PER BOOKS</u>	<u>NET INVESTMENT INCOME</u>	<u>ADJUSTED NET INCOME</u>	<u>CHARITABLE PURPOSES</u>
LEGAL	205.			205.
TOTALS	<u>205.</u>	<u>0.</u>	<u>0.</u>	<u>205.</u>

ATTACHMENT 3

FORM 990PF, PART I - ACCOUNTING FEES

<u>DESCRIPTION</u>	<u>REVENUE AND EXPENSES PER BOOKS</u>	<u>NET INVESTMENT INCOME</u>	<u>ADJUSTED NET INCOME</u>	<u>CHARITABLE PURPOSES</u>
ACCOUNTING	13,313.	9,319.		3,994.
TOTALS	<u>13,313.</u>	<u>9,319.</u>	<u>0.</u>	<u>3,994.</u>

ATTACHMENT 4

FORM 990PF, PART I - TAXES

<u>DESCRIPTION</u>	<u>REVENUE AND EXPENSES PER BOOKS</u>	<u>NET INVESTMENT INCOME</u>	<u>CHARITABLE PURPOSES</u>
PAYROLL TAXES	15.	5.	10.
TOTALS	<u>15.</u>	<u>5.</u>	<u>10.</u>

ATTACHMENT 5

FORM 990PF, PART I - OTHER EXPENSES

<u>DESCRIPTION</u>	REVENUE AND EXPENSES <u>PER BOOKS</u>
BANK CHARGES	90.
TOTALS	<u>90.</u>

CHARITABLE PURPOSES	90.
	<u>90.</u>

THE NOTSEW ORM SANDS FOUNDATION

76-0455176

FORM 990PF, PART II - OTHER LIABILITIES

ATTACHMENT 6

<u>DESCRIPTION</u>	<u>ENDING BOOK VALUE</u>
PAYROLL WITHHOLDINGS PAYABLE	400.
TOTALS	<u>400.</u>

THE NOTSEW ORM SANDS FOUNDATION

76-0455176

ATTACHMENT 7

FORM 990PF, PART VII-A, LINE 14 - LOCATION OF BOOKS

22 ST. CLAIR AVENUE EAST, SUITE 500 TORONTO
ONTARIO CANADA

ATTACHMENT 8

FORM 990PF, PART VII-B, LINE 5C-EXPENDITURE RESPONSIBILITY STATEMENT

GRANTEE'S NAME: STANDEN, LTD.
GRANTEE'S ADDRESS: LE MASURIER HOUSE, LARUE DE MASURIER JE2
CITY, STATE & ZIP: ST. HELIER
FOREIGN PROVINCE: JERSEY
FOREIGN COUNTRY: JERSEY
GRANT DATE: 01/31/2008
GRANT AMOUNT: 2,000,000.
GRANT PURPOSE: SEE ATTACHED GRANT DOCUMENT
AMOUNT EXPENDED: 2,000,000.
ANY DIVERSION? NO
DATES OF REPORTS: SEE ATTACHED GRANTEE REPORTING
VERIFICATION DATE:
RESULTS OF VERIFICATION:

THE NOTSEW ORM SANDS FOUNDATION

76-0455176

FORM 990PF, PART VIII - LIST OF OFFICERS, DIRECTORS, AND TRUSTEES

ATTACHMENT 9

<u>NAME AND ADDRESS</u>	<u>TITLE AND AVERAGE HOURS PER WEEK DEVOTED TO POSITION</u>	<u>COMPENSATION</u>
CHARLES BURNETT III 1535 E POTOMAC HOUSTON, TX 77057	PRES/SEC 6.00	5,000.
GARFIELD MITCHELL 22 ST. CLAIR AVE. E., STE. 1901 M4T2S8 TORONTO ONTARIO CANADA	DIRECTOR	
GRAHAM WESTON 112 E. PECAN ST. BOX 6 SAN ANTONIO, TX 78205	DIRECTOR	
MELISSA BARON MURDOCK 2470 S. DIARY ASHFORD # 802 HOUSTON, TX 77077	DIRECTOR	
PILAR BAUTA 2470 S. DIARY ASHFORD # 802 HOUSTON, TX 77077	DIRECTOR	
GRAND TOTALS		<u>5,000.</u>

THE NOTSEW ORM SANDS FOUNDATION
EIN: 76-0455176

ATTACHMENT 10 TO FORM 990-PF, PART XV, LINE 2

- 2a: BOARD OF DIRECTORS
THE NOTSEW ORM SANDS FOUNDATION
2470 S. DAIRY ASHFORD, #802
HOUSTON, TX 77077
(281) 497-0744
- 2b: ORGANIZATIONS SEEKING GRANTS SHOULD SUBMIT AN OUTLINE OF THE PROPOSED PROGRAM AND A PROPOSED BUDGET, AS WELL AS ANY OTHER INFORMATION REQUIRED BY THE NOTSEW ORM SANDS FOUNDATION BOARD OF DIRECTORS.
- 2c: APPLICATIONS ARE ACCEPTED AT ANY TIME. NOTICE OF APPROVAL, REJECTION OR REQUESTS FOR ADDITIONAL INFORMATION ARE USUALLY SENT WITHIN 90 DAYS.
- 2d: GRANTS ARE AWARDED AT BOARD OF DIRECTOR DISCRETION TO ORGANIZATIONS WITH PROGRAMS SUPPORTING THE FURTHERANCE OF CHARITABLE, SCIENTIFIC OR EDUCATIONAL PURPOSES WITHIN THE MEANING OF IRC SECTION 501(c)(3).

THE FOUNDATION MAKES CONTRIBUTIONS ON A REGULAR BASIS TO QUALIFIED SECTION 501(c)(3) CHARITIES AT THE DISCRETION OF THE FOUNDATION'S BOARD OF DIRECTORS.

FORM 990-BE, PART XV - GRANTS AND CONTRIBUTIONS PAID DURING THE YEAR

ATTACHMENT 11

<u>RECIPIENT NAME AND ADDRESS</u>	<u>RELATIONSHIP TO SUBSTANTIAL CONTRIBUTOR AND FOUNDATION STATUS OF RECIPIENT</u>	<u>PURPOSE OF GRANT OR CONTRIBUTION</u>	<u>AMOUNT</u>
FRIENDS OF HOLLYWOOD CEMETERY 412 SOUTH CHERRY STREET RICHMOND, VA 23220	NONE	GENERAL CHARITABLE DONATION	5,000.
HOUSTON SPCA 900 PORTWAY DRIVE HOUSTON, TX 77024	NONE	GENERAL CHARITABLE DONATION	5,000
THE ENERGY TRANSFER TRUST 4 FELSTEAD GARDENS E14 3BS FERRY STREET LONDON UNITED KINGDOM	NONE	GENERAL CHARITABLE DONATIONS	919,258.
TOTAL CONTRIBUTIONS PAID			<u>929,258.</u>



November 5, 2010

Notsew Orm Sands Foundation
50 Briar Hollow Lane, 590E
Houston, Texas 77027

Re: 2009 Annual Report to Support the Grant Agreement Between Notsew Orm Sands Foundation and Standen, Ltd.

Dear Notsew Orm Sands Foundation:

Pursuant to the terms of the Grant Agreement and subsequent Addendum between Notsew Orm Sands Foundation and Standen, Ltd., Standen Ltd. and its wholly owned subsidiary NovoCure Ltd. submit this annual report to account for our expenses associated with the grant and provide an update on the progress of the effort.

The purpose of the January 2008 grant was to promote the development of potentially life-saving treatments for patients with cancerous tumors by helping to fund the early clinical testing of NovoCure Ltd.'s treatment for newly diagnosed glioblastoma multiforme (GBM) patients in the USA.

In 2008 the company was granted Investigational Device Exemption (IDE) #G070228 by the US Food and Drug Administration (FDA) to conduct a prospective, randomized, multi-center trial of the NovoTTF-100A in conjunction with temozolomide versus temozolomide alone in patients with newly diagnosed GBM (Protocol EF-14).

The activities for the year 2009 directly applicable to the execution of the trial were:

- Working with our Contract Research Organization (CRO) partner, Ockham Development Group (Ockham) to develop the clinical reporting forms, investigator manual, and other supporting documentation including an implementation of an Electronic Data Collection (EDC) system for the trial.
- Also with the CRO, Ockham, we initiated the recruitment of research sites (hospitals) to join the trial and prepared and initiated the associated regulatory filings. Ten clinical trial sites were opened in 2009.
- Manufacturing of NovoTTF-100A devices and associated electrodes to support the treatment of trial patients.
- Recruited, hired, and trained an additional four technicians and open four new technical centers to support the trial, bringing the total number of US technicians and technical centers to ten.
- Enrolled first patient in the trial on July 15, 2009. Enrolled and supported 16 US patients (27 worldwide) in 2009.

NovoCure Ltd.

Topaz Bldg, 4th floor, Shaa'r HaCarmel
P.O. Box 15022 MATAM Center, Haifa 31905
Tel 972 4 8501204; Fax: 972 4 8501207



The expenses covered by the grant for 2009 correlate with the above activities (Attachment 1). A total of \$1,866,480 was spent on the above activities of which \$1,512,773 was spent from the grant funds. A detailed accounting of the expenditures is found in the referenced Attachment.

The combination of the 2009 grant expenses along with the 2008 expenses of \$487,227 brings the total grant expenses used for the trial to \$2,000,000.

The list of trial sites and dates opened is found in Attachment 2.

The plans for the newly diagnosed GBM EF-14 trial for 2010 include:

- Continuing to manufacture equipment and supplies for use by trial patients.
- Work with our CRO, Ockham, to open at least 7 additional US sites.
- Continue to recruit and enroll trial patients, working toward completing the goal of 283 patients enrolled by year end of 2011.
- Provide technical, clinical, and operational support to the patients under treatment on the trial.

With this report, we certify that we are in full compliance with the terms of the Grant Agreement with the exception of the timing of the filing of this report.

We would like to thank the Notsew Orm Sands Foundation for their generous support of our research program. With the use of this grant we have made great strides in accelerating our Newly Diagnosed GBM Clinical Trial and are well on our way to completing the trial enrollment in 2011.

Sincerely,

Asaf Danziger
CEO, NovoCure Ltd.

List of Attachments:

Attachment 1 – Expenses for the 2009 period

Attachment 2 – List of EF-14 US Clinical Trial Sites

NovoCure Ltd.

Topaz Bldg. 4th floor, Shaa'r HaCarmel
P.O. Box 15022 MATAM Center, Haifa 31905
Tel: 972 4 8501204; Fax 972 4 8501207.

ATTACHMENT 1: EXPENSES FOR 2009 PERIOD

Standen Ltd

Newly diagnosed GBM (EF14 Project)

Expenses report for the year 2009

Expenses	Supplier	Amount (\$)
<u>Electronic Materials</u>		
	AL Electronics Ltd.	\$280,725
	Minnesota Wire & Cable Co.	\$31,148
	ITT Corporation (EDO)	\$308,587
<u>Contract Research Organization (CRO)</u>		
	Ockham Development Group, Inc.	\$466,230
<u>Clinical Trial Sites</u>		
	Medical Center Payments	\$156,190
<u>Manpower</u>		
	<u>NovoCure Ltd.</u>	
	Chief Medical Officer	\$89,308
	Medical Director	\$27,980
	<u>Standen Inc. USA</u>	
	Clinical Trial Management	\$237,612
	Technician Supervisor	\$58,261
	Technician-Chicago	\$20,621
	Technician-Pittsburgh	\$20,870
	Technician-New York	\$31,014
	Technician- Boston	\$31,077
	Technician -New Hampshire	\$23,847
	Technician-Dallas	\$27,769
	Technician-San Diego	\$23,515
	Technician-Orlando	\$22,294
	Technician-Danville, PA	\$9,431
	Total	\$1,866,480

Prepared by Hanan Herscovitch, CFO
Standen Ltd

Date November 5th, 2010

ATTACHMENT 1: EXPENSES FOR 2009 PERIOD

Explanation of Expenses:

Electronic Materials

ALE Electronic Ltd. - contract manufacturer for the NovoTTF-100A device and the electronic assembly portion of the electrodes used in the US for the trial

Minnesota Wire & Cable - manufacturer of electrode cables and device connection cables used in the US for the trial

EDO Corporation - manufacturer of the custom ceramics for the electrodes to be used in the US for the trial

Contract Research Organization (CRO):

Ockham Development Group, Inc. - CRO for the US trial, fees for designing and implementing the Electronic Clinical Reporting Forms, supporting trial site regulatory filings, and monitoring trial activities at the sites.

Clinical Trial Sites:

Medical Center Payments - payments to medical institutions participating in the study for patient screening, enrollment, and follow up.

Manpower

Chief Medical Officer - Eilon Kirson, MD, PhD - a portion of Dr Kirson's time for supporting regulatory filings and site openings in the US

Medical Director - Un Weinberg, MD, PhD - a portion of Dr Weinberg's time supporting US trial sites as the medical director for the trial

Clinical Trial Management - Mike Ambrogio, COO and staff - a portion of Mr Ambrogio's time and support staff time for direct US trial management

Technician Supervisor and Site Technicians - direct technical support of US clinical trial patients

ATTACHMENT 2. US Clinical Trial Sites

Standen Ltd

Newly diagnosed GBM (EF14 Project)

US Clinical Trial Sites

	Site	Principal Investigator	Opened
1	University of Illinois at Chicago	Herb Engelhard, MD, PhD	June 2009
2	MDA Anderson Cancer Center Orlando	Nicholas Avgeropoulos, MD	June 2009
3	Tufts Medical Center	J. Scott Nystrom, MD	June 2009
4	Baylor Health Center	Karen Fink, MD, PhD	June 2009
5	Maine Medical Center	Rajiv Desai, MD	June 2009
6	NJ Neuroscience Institute	Joseph Landolfi, DO	June 2009
7	University of Pittsburgh Medical Center	Frank Lieberman, MD	July 2009
8	Weill Cornell Medical School	Susan Pannullo, MD	July 2009
9	University of California San Diego	William Read, MD	July 2009
10	Geisinger Health Center	Steven Toms, MD	July 2009
11	University of Southern California	Thomas Chen, MD, PhD	March 2010
12	Swedish Medical Center	John Henson, MD	March 2010
13	Moffitt Cancer Center	Steven Brem, MD	June 2010
14	Lahey Clinic	Carlos David, MD	July 2010
15	University of North Carolina	Matthew Ewend, MD	July 2010
16	Methodist Hospital	Pamela New, MD	September 2010
17	Yvonne Kew MD PLLC	Yvonne Kew, MD, PhD	September 2010
18	Beth Israel Deaconess Medical Center	Eric Wong, MD	Pending
19	Cleveland Clinic	Robert Weil, MD	Pending

GRANT AGREEMENT

This Grant Agreement is made as of January __, 2008 (the "Agreement") between (1) Notsew Orm Sands Foundation (the "Foundation"), with its principal offices located at 50 Briar Hollow Lane, 590E, Houston, Texas 77027, and (2) Standen Ltd., a company organized under the laws of Jersey (the "Grantee"), with an office located at Le Masurier House, La Rue le Masurier, St. Helier, Jersey JE2 4YE.

RECITALS:

A. The Foundation is a Texas non-profit corporation, organized for charitable, scientific, and educational purposes within Section 501(c)(3) of the United States Internal Revenue Code ("I.R.C. §501(c)(3)").

B. The Grantee is an early stage medical device company whose scientists and engineers have invented and developed a new medical device for treating cancerous tumors known as the NovoTTF (the "Device"), which Device is currently being investigated pursuant to an investigational device exemption ("IDE") issued by the U.S. Food and Drug Administration ("FDA"), for the clinical study of the safety and efficacy of the Device in treating patients with recurrent glioblastoma multiforme ("GBM"):

C. In furtherance of its I.R.C. §501(c)(3) purpose, the Foundation wishes to promote the development of life-prolonging treatments for patients with cancerous tumors. Specifically, the Foundation wishes to advance the further investigation of the Device and its potential availability to patients by funding a portion of the expansion of the clinical study of the Device to determine its safety and efficacy on patients with newly diagnosed GBM, and

D. In order to evidence the parties' respective obligations hereunder, and as a condition of the Grantee's receipt of funds from the Foundation, the parties are entering into this Agreement.

Accordingly, in consideration of the mutual covenants contained in this Agreement, and intending to be legally bound hereby, the Foundation and the Grantee hereby agree as follows.

1. Grant and Use of Funds.

(a) The Foundation hereby agrees to make a grant to Grantee in the amount of Two Million Dollars (\$2,000,000) (the "Grant Funds") within five days of the date of this Agreement (the "Payment Date"), subject to the terms and conditions contained herein.

(b) The Grantee agrees to use the Grant Funds (including any interest income accruing thereon prior to their use by the Grantee) for purposes of paying any costs and expenses related to the clinical study of the use of the Device in patients with newly diagnosed GBM.

including as part of an FDA-approved IDE in the United States, and as part of a multi-center worldwide pivotal clinical trial, and all activities necessarily related thereto (the "Project"). The Grantee agrees that the Grant Funds shall not be used for any purpose other than the Project. In the event that the Grant Funds are not used or committed to be used by the Grantee in the Project within five years following the Payment Date then the Grantee shall return such unused Grant Funds to the Foundation.

(c) The Grant Funds shall be paid to the account designated on Schedule 1 hereto (the "Project Account"), and the Grantee shall at all times maintain the Grant Funds in the Project Account as a separate and segregated account solely for the purpose of the Project

(d) Grantee agrees that the Grant Funds will not be used to carry on propaganda or otherwise to attempt to influence legislation or the outcome of any specific public election or to carry on a voter registration drive

(e) The Grantee shall not be entitled to use the Grant Funds to make charitable grants to another organization, provided that nothing in this paragraph (e) shall prevent the Grantee from compensating not-for-profit academic or medical institutions for their participation and conduct of clinical research as part of the Project

2. Reports.

(a) The Grantee must provide an annual narrative and financial report to the Foundation no later than ninety (90) days following the close of each of Grantee's fiscal years in which the Grantee spends any portion of the Grant Funds.

(b) The narrative portion of each report must include: (1) a copy of each professional publication, submission to government regulatory agencies, and other material produced by the Grantee that describes the activities being planned, and conducted by Grantee in connection with the Project; and (2) a certification as to the Grantee's compliance with the terms of this Agreement.

(c) The financial portion of each annual report furnished by Grantee must be attested to by an accountant and must contain an explanation of all expenditures using Grant Funds, such as for salaries, regulatory submissions, data analysis, travel, supplies and the like.

(d) When the Grant Funds are fully exhausted, the Grantee must provide a final report that lists the expenditures made from Grant Funds and details the progress the Grantee has made toward achieving the goals of the Project.

(e) Records of receipts and expenditures relating to Grant Funds, as well as the Grantee's books and records, and copies of any narrative and financial reports furnished to the Foundation, must be kept by or on behalf of the Grantee. The Grantee shall make such books and records available for inspection by the Foundation, upon reasonable advance notice and during regular business hours, during any time period before the Grant Funds are fully exhausted, and for at least three (3) years thereafter

(f) Without limiting the foregoing, the parties agree to take such actions, including amendment of this Agreement, as may be reasonably required to enable the Grantor to exercise expenditure responsibility within the meaning of Section 4945 of the United States Internal Revenue Code and the regulations thereunder.

3 Termination The Foundation shall have the authority to terminate this Agreement, and to hold or recover Grant Funds in cases where Grant Funds are being used other than for purposes of the Project, as determined in the reasonable discretion of the Foundation

4. Non-Disclosure. Neither party to this Agreement may use the name of the other party to this Agreement in connection with any press release or publicity, except upon the prior written consent of such other party. The Foundation agrees to keep the existence of this Agreement and its terms and any information that the Foundation receives regarding the Project in strict confidence, and not to disclose any such information to anyone but its legal and financial advisors, who require such information, and who are bound by confidentiality obligations. Nothing herein shall be deemed to prevent or limit Foundation from including a description of the grant to the Grantee of the Grant Funds on the Foundation's annual information return to the United States Internal Revenue Service. Further, nothing herein shall prevent either party from making any other disclosures that are required by applicable law or regulation, provided that such party provides advance notice to the other party of the nature of such planned disclosure, and provides the other party with an opportunity to seek legal means to limit such disclosure.

5 Certain Representations.

(a) The Grantee hereby represents and warrants to the Foundation that: (1) the Grantee is a legal entity duly organized, validly existing and in good standing, and has the power to own its property and to carry on its business as now being conducted by it, (2) the execution and delivery of this Agreement and the consummation of the transactions contemplated herein by the Grantee, have been duly authorized by all necessary action by the Grantee; and (3) during the term of this Agreement, the Grantee shall take all actions necessary and appropriate to assure that it and its agents and employees comply with all laws and regulations applicable to the Grantee in connection with the use of the Grant Funds

(b) The Foundation hereby represents and warrants to the Grantee that, (1) the Foundation is a legal entity duly organized, validly existing and in good standing, and has the power to own its property and to carry on its business as now being conducted by it, and (2) the execution and delivery of this Agreement and the consummation of the transactions contemplated herein by the Foundation, have been duly authorized by all necessary action by the Foundation

(c) The Grantee hereby certifies that it does not employ or deal with any entity or individual known to support terrorism or any entity or individual on any list of the U S government, the United Nations or the European Union identifying such persons as having links to terrorism or to money laundering, and that the Grantee will take reasonable steps to ensure that Grant Funds are not ultimately distributed to terrorist organizations

6 Miscellaneous.

(a) Notices. All notices, claims, demands and other communications hereunder shall be in writing and shall be deemed given if delivered personally or by telex or telecopier, one business day after being sent by major overnight courier, or four business days after being mailed by registered or certified mail (postage prepaid, return receipt requested) to each party at its respective address set forth in the preamble to this Agreement or at such other address that is specified in advance by the respective party.

(b) Entire Agreement. This Agreement constitutes the entire agreement and supersedes all other prior agreements and understandings, both written and oral, among the parties or any of them, with respect to the subject matter hereof.

(c) Governing Law; Submission to Jurisdiction. This Agreement shall be governed by and construed and enforced in accordance with the internal laws of the United States and the State of Texas. The parties agree to the non-exclusive jurisdiction and venue in any action brought by any party pursuant to this Agreement in any federal or state court located in the State of Texas and County of Harris. By execution and delivery of this Agreement, each party irrevocably submits to the jurisdiction of such courts for itself and in respect of his or its property with respect to such action. The parties irrevocably agree that venue would be proper in any such court, and hereby waive any objection that such court is an improper or inconvenient forum for the resolution of such action. The parties further agree that the mailing by certified or registered mail, return receipt requested, of any process required by any such court shall constitute valid and lawful service of process against them, without necessity for service by any other means provided by statute or rule of court.

(d) Waiver of Jury Trial. EACH OF THE PARTIES HEREBY KNOWINGLY, VOLUNTARILY, AND INTENTIONALLY WAIVES ANY RIGHTS IT MAY HAVE TO A TRIAL BY JURY IN RESPECT OF ANY LITIGATION BASED UPON, OR ARISING OUT OF, UNDER OR IN CONNECTION WITH, THIS AGREEMENT, ANY OTHER AGREEMENTS BETWEEN THE PARTIES OR ANY COURSE OF CONDUCT, COURSE OF DEALING, STATEMENTS (WHETHER ORAL OR WRITTEN) OR ACTIONS OF THE PARTIES.

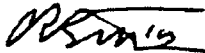
(e) Counterparts. This Agreement may be executed in one or more counterparts, each of which shall be deemed to be an original but all of which shall constitute one and the same agreement

IN WITNESS WHEREOF, the parties have duly executed and delivered this Agreement -----
on and as of the date first above written.

STANDEN LTD.


NOTSEW ORM SANDS FOUNDATION

By: _____
Name: Asaf Danzinger
Title: CEO
Dated:

By:  _____
Name: Charles Burnett, III
Title: President
Dated:

STATE OF TEXAS, County of [illegible]

IN WITNESS WHEREOF, I have hereunto set my hand and seal of office at the City of [illegible] this [illegible] day of [illegible] 20[illegible].

BY: 
[illegible]
[illegible]
[illegible]

IN WITNESS WHEREOF, I have hereunto set my hand and seal of office at the City of [illegible] this [illegible] day of [illegible] 20[illegible].

✓

GRANT AGREEMENT ADDENDUM

This Grant Agreement Addendum ("Addendum") is entered into effective as of January __, 2008. This Addendum clarifies the agreement between (1) Notsew Orm Sands Foundation (the "**Foundation**"), and (2) Standen Ltd. (the "**Grantee**") (the Foundation and the Grantee collectively are referred to as the "**Parties**") as set forth in the Parties' Grant Agreement dated January __, 2008 (the "**Grant Agreement**").

RECITALS:

A. The Grantee's scientists and engineers have developed a new medical device (the "**Device**") that is currently being investigated pursuant to an investigational device exemption ("**IDE**") issued by the U.S. Food and Drug Administration ("**FDA**").

B. The Foundation has agreed to make a grant to Grantee in the amount of Two Million Dollars (\$2,000,000) (the "**Grant Funds**"), subject to the terms and conditions contained in the Grant Agreement.

C. The Grant Agreement provides that the Grantee will use the Grant Funds (including any interest income accruing thereon prior to their use by the Grantee) for purposes of paying any costs and expenses related to the clinical study of the use of the Device in patients with newly diagnosed GBM, including as part of an FDA-approved IDE in the United States, and as part of a multi-center worldwide pivotal clinical trial, and all activities necessarily related thereto.

D. The clinical study is being conducted by Standen USA, Inc., a United States corporation wholly-owned by Grantee.

E. The Parties intend that all Grant Funds (including any interest income accruing thereon prior to their use by the Grantee) be used by or for the benefit of Standen USA, Inc., in furtherance of the clinical study and that no part of the Grant Funds or interest income accruing thereon be used by the Grantee for any other purpose.

F. The Parties wish to resolve any ambiguity that may exist in the Grant Agreement as originally entered into.

Accordingly, in consideration of the mutual covenants contained in this Addendum, and intending to be legally bound hereby, the Foundation and the Grantee hereby agree as follows:

1. Clarifying Revisions to Grant Agreement.

(a) Section 1(b) of the Grant Agreement shall be, and hereby is, revised to read in its entirety as follows:

The Grantee agrees to use the Grant Funds (including any interest income accruing thereon prior to their use by the Grantee) for purposes of paying any costs and expenses incurred by Standen USA, Inc. related to the clinical study of the use of the Device in patients with newly diagnosed GBM, including as part of an FDA-approved IDE in the United States, and as part of a multi-center worldwide pivotal clinical trial, and all activities necessarily related thereto (the "**Project**"). The Grantee agrees that the Grant Funds shall not be used for any purpose other than the Project. In the event that the Grant Funds are not used or committed to be used by the Grantee in the Project within five years following the Payment Date then the Grantee shall return such unused Grant Funds to the Foundation.

(b) Section 1(c) of the Grant Agreement shall be, and hereby is, revised to read in its entirety as follows:

Solely for ease of administerability, the Grant Funds may be paid directly to Grantee, to be remitted to or paid on behalf of Standen USA, Inc , in furtherance of the Project. Pending disbursement in furtherance of the Project, the Grant Funds shall be paid to the account designated on Schedule 1 hereto (the "**Project Account**"), and the Grantee shall at all times maintain the Grant Funds in the Project Account as a separate and segregated account solely for the purpose of the Project. Grantee shall have no right to use any Grant Funds not remitted to Standen USA, Inc. except to make payments on behalf of Standen USA, Inc. in furtherance of the Project.

2. Ratification and Confirmation. In all other respects, the Parties ratify and confirm the provisions of the Grant Agreement as originally entered into.

3. Joining of Standen USA, Inc. By its signature hereto, Standen USA, Inc. agrees to be bound by the terms of the Grant Agreement and this Addendum to the same extent that the Grantee is bound by same.

IN WITNESS WHEREOF, the Parties and Standen USA Inc. have duly executed and delivered this Addendum effective as of the date first above written

STANDEN LTD

NOTSEW ORM SANDS FOUNDATION

By *Asaf Danziger*
Name: Asaf Danziger
Title: CEO

By *Charles Burnett, III*
Name: Charles Burnett, III
Title: President

STANDEN USA, INC

By *Michael Ambrogio*
Name: Michael Ambrogio
Title: COO

✓



March 19, 2010

Notsew Orm Sands Foundation
50 Briar Hollow Lane, 590E
Houston, Texas 77027

Re: 2008 Annual Report to Support the Grant Agreement Between Notsew Orm Sands Foundation and Standen, Ltd.

Dear Notsew Orm Sands Foundation:

Pursuant to the terms of the Grant Agreement and subsequent Addendum between Notsew Orm Sands Foundation and Standen, Ltd., Standen Ltd. and its wholly owned subsidiaries NovoCure Ltd. and Standen USA Inc. submit this annual report to account for our expenses associated with the grant and provide an update on the progress of the effort.

The purpose of the January 2008 grant was to promote the development of potentially life-saving treatments for patients with cancerous tumors by helping to fund the early clinical testing of NovoCure Ltd.'s treatment for newly diagnosed glioblastoma multiforme (GBM) patients in the USA.

In 2008 the company was granted Investigational Device Exemption (IDE) #G070228 by the US Food and Drug Administration (FDA) (Attachment 1) to conduct a prospective, randomized, multi-center trial of the NovoTTF-100A in conjunction with temozolomide versus temozolomide alone in patients with newly diagnosed GBM (Protocol EF-14).

The activities for the year directly applicable to the execution of the trial in the USA were:

- Initiated the manufacturing of NovoTTF-100A devices and associated electrodes
- Collaborated with the US trial sites to initiate the process of opening the trial
- Worked with US FDA on trial administration

The expenses covered by the grant for 2008 correlate with the above activities (Attachment 2). A total of \$487,227 was spent from the grant funds. A detailed accounting of the expenditures is found with the attachment.

Also in 2008, Dr. Eilon Kirson, VP of R&D for NovoCure, made a presentation of our pilot trial results with newly diagnosed GBM patients at the annual meeting of the Society of Neuro Oncology. A copy of the abstract for his presentation is found in Attachment 3.

A peer-reviewed publication of our pre-clinical and clinical work on treatments that combine the NovoTTF-110A with chemotherapy, including our newly diagnosed

NovoCure Ltd.

Topaz Bldg. 4th floor, Shaa'r HaCarmel
P O. Box 15022 MATAM Center, Haifa 31905
Tel 972 4 8501204, Fax 972 4 8501207



GBM pilot trial was developed in 2008. The publication appeared in the January edition of BMC Medical Physics and is attached as Attachment 4.

The plans for the newly diagnosed GBM EF-14 trial for 2009 include:

- Continuing to manufacture equipment and supplies for use by trial patients.
- Work with our US CRO, Ockham Development Group (Ockham), to develop, test, and deploy the electronic databases to collect and control trial data.
- Work with Ockham to complete the required Institutional Review Board (IRB) regulatory filings, initiate, and train trial sites.
- Develop website, video, and printed material for patient recruitment.
- Open the trial in at least 10 US sites and initiate recruitment.
- Provide technical, clinical, and operational support to the patients under treatment on the trial.

As of the date of this report, we have opened the trial at 10 US centers and recruited our first thirty patients into the study. The complete list of trial sites can be found in Attachment 5.

With this report, we certify that we are in full compliance with the terms of the Grant Agreement with the exception of the timing of the filing of this report. We apologize for the delay and will make sure the reports for subsequent years are filed within the window outlined in the agreement.

We are very thankful for the support provided by the Notsew Orm Sands Foundation. We could not be moving so quickly to initiate this critical trial without your help.

Sincerely,

Asaf Danziger

CEO, NovoCure Ltd.

cc: Mr. Charles Burnett via email
Attachments

List of Attachments:

- Attachment 1 – FDA letter granting the IDE for the trial
- Attachment 2 – Expenses for the 2008 period
- Attachment 3 – Abstract for Society of Neuro Oncology (SNO) presentation
- Attachment 4 – Medical Physics publication
- Attachment 5 – List of EF-14 trial sites

NovoCure Ltd.

Topaz Bldg. 4th floor, Shaa'r HaCarmel
P O. Box 15022 MATAM Center, Haifa 31905
Tel: 972 4 8501204; Fax: 972 4 8501207

ATTACHMENT 1 - FDA IDE APPROVAL EF-14



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

NovoCure, Ltd.
% Hogan & Hartson LLP
Mr. Jonathan S. Kahan
555 Thirteen Street, Northwest
Washington, District of Columbia 20004

MAY 28 2008

Re: G070228/S3
NovoTTF-100A System
Indications for Use: treatment of newly diagnosed Glioblastoma Multiforme (GBM)
Dated: April 29, 2008
Received: April 29, 2008
CMS Reimbursement Category: B1
Annual Report Due: One Year from the Date of This Letter

Dear Mr Kahan:

The Food and Drug Administration (FDA) has reviewed the supplement to your investigational device exemptions (IDE) application. You have corrected the deficiencies cited in our April 4, 2008 conditional approval letter. Therefore, your supplement is approved and you may continue your investigation at the institutions enrolled in your investigation after you have obtained institutional review board (IRB) approval and submitted certification of IRB approval to FDA. Your investigation is limited to 25 institutions and 283 subjects.

We would like to point out that FDA approval of your IDE application does not imply that this investigation will develop sufficient safety and effectiveness data to assure a determination of substantial equivalence of a premarket notification (510(k)) submission / FDA approval of a premarket approval (PMA) application for this device. You may obtain guidance for the preparation of a PMA application from our Device Advice website (<http://www.fda.gov/cdrh/devadvice/pma>) or from the Division of Small Manufacturers, International and Consumer Assistance at toll-free number (800) 638-2041 or (240) 276-3150.

Future correspondence concerning this application should be identified as an IDE supplement referencing the IDE number above, and must be submitted in triplicate to:

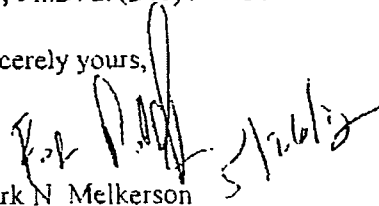
IDE Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

ATTACHMENT 1 - FDA IDE APPROVAL EF-14

Page 2 - Mr. Jonathan S Kahan

If you have any questions, please contact Long Chen, Ph.D. at (240) 276-3600.

Sincerely yours,



Mark N Melkerson
Director
Division of General, Restorative
and Neurological Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

ATTACHMENT 2: EXPENSES FOR 2008 PERIOD

Standen Ltd

Newly diagnosed GBM (EF14 Project)

Expenses report for the year 2008

Expenses*	Supplier	Date	Invoice #	Amount (\$)
<u>Electronic Materials</u>				
	AL Electronics Ltd.	12/1/2008	36451	\$23,333
	AL Electronics Ltd.	12/1/2008	36452	\$2,644
	AL Electronics Ltd.	12/4/2008	36526	\$339
	EDO Corporation	12/15/2008	9728	\$47,400
	EDO Corporation	12/2/2008	9641	\$47,400
	EDO Corporation	11/13/2008	9596	\$47,400
	EDO Corporation	11/4/2008	9531	\$47,400
	EDO Corporation	10/27/2008	9502	\$47,400
	EDO Corporation	10/16/2008	9439	\$47,400
	EDO Corporation	8/25/2008	9092	\$47,400
	EDO Corporation	9/30/2008	9319	\$47,400
	EDO Corporation	9/5/2008	9191	\$47,400
<u>Manpower</u>				
	Eilon Kirson-Payroll Expenses	6/30/2008		\$7,448
	Eilon Kirson-Payroll Expenses	7/30/2008		\$4,674
	Eilon Kirson-Payroll Expenses	8/30/2008		\$4,523
	Eilon Kirson-Payroll Expenses	9/30/2008		\$4,773
	Eilon Kirson-Payroll Expenses	10/30/2008		\$4,387
	Eilon Kirson-Payroll Expenses	11/30/2008		\$4,188
	Eilon Kirson-Payroll Expenses	12/30/2008		\$4,319
Total				\$487,227

* See accompanying explanation of expense items

Prepared by Hanan Herscovitch, CFO
Standen Ltd

Date June 1, 2009

Explanation of Expenses:

Electronic Materials

ALE Electronic Ltd - contract manufacturer for the NovoTTF-100A device and the electronic assembly portion of the electrodes to be used in the US for the trial

EDO Corporation - manufacturer of the custom ceramics for the electrodes to be used in the US for the trial

Manpower

Dr Eilon Kirson, VP of R&D - a portion of Dr Kirson's time for trial planning and preparation of regulatory filings

ATTACHMENT 3 – SNO ABSTRACT

Abstracts for the Thirteenth Annual Meeting of the Society for Neuro-Oncology
November 20–23, 2008

ET-03. THE EFFICACY OF TEMOZOLOMIDE IN VITRO AND IN PATIENTS WITH NEWLY DIAGNOSED GBM IS ENHANCED BY ADJUVANT EXPOSURE TO ALTERNATING ELECTRIC FIELDS (TTFIELDS)

Eilon Kirson¹, Vladimir Dbaly², Frantisek Tovarys², Josef Vymazal³, Rosa Schneiderman⁴, Yoram Wasserman⁵, and Yoram Palti¹; ¹NovoCure Ltd., Haifa, Israel, ²Neurosurgery, Na Homolce Hospital, Prague, Czech Republic; ³Radiology, Na Homolce Hospital, Prague, Czech Republic, ⁴Biology, NovoCure Ltd., Haifa, Israel, ⁵Engineering, NovoCure Ltd., Haifa, Israel

BACKGROUND Alternating electric fields (TTFields) have been shown to exert anti-tumor activity, destroying cycling cells during mitosis. Preliminary clinical experience suggests efficacy against recurrent glioma; this technique is currently undergoing phase III evaluation in patients with recurrent glioblastoma. In vitro synergy with various chemotherapeutic agents has been shown in breast and lung cancer cell lines (Kirson et al, AACR 2007).

METHODS: In the present study, the effects of TTFields alone and in combination with DTIC were tested in human glioma (GBM) cells in vitro (U-87). Subsequently, the effects of TTFields in combination with maintenance temozolomide (TMZ) were tested in an open-label, single-arm, prospective, pilot clinical trial. Ten patients (median age 54 years, KPS > 70, gross total tumor resection in 4 patients [40%]) with newly diagnosed GBM were treated with standard TMZ/RT. During the maintenance TMZ administration, TTFields were applied continually (18 hours a day, on average) for up to 18 months. All patients were followed on a monthly basis (including monthly contrast magnetic resonance imaging of the brain). The primary endpoints were feasibility and toxicity, time to disease progression, and overall survival. Results were compared to concurrent and historical controls.

RESULTS: In vitro, full additivity of the inhibitory effects of DTIC and TTFields was observed when both treatments were applied concomitantly to GBM cells in culture. This finding was true for all DTIC concentrations tested. In the pilot clinical trial, no device-related, systemic, adverse events were noted throughout the treatment with TTFields (cumulative treatment time more than 170 months; median administration time 12 months). Over time, a mild to moderate skin irritation appeared beneath the electrode gel in all patients. Median time to disease progression was 155 weeks in patients treated with combined TMZ and TTFields, compared to 31 weeks in concurrent control patients treated with TMZ alone (hazard ratio 3.7, 95% confidence interval 2.1–6.7). Half the patients were still progression-free at the end of the trial. Median overall survival was 40 months in patients treated with combined TMZ and TTFields, compared to 14.7 months reported for historical controls (Stupp et al. 2004). Eight of the 10 patients were still alive at the end of this study.

CONCLUSIONS: These promising findings suggest that TTFields can be applied over many months without significant toxicity. The combination with standard TMZ chemotherapy may greatly enhance the anti-tumor effect of TMZ translating into prolonged time to progression and survival.

Research article



Chemotherapeutic treatment efficacy and sensitivity are increased by adjuvant alternating electric fields (TTFields)

Eilon D Kirson^{*1}, Rosa S Schneiderman¹, Vladimír Dbalý²,
František Továryš², Josef Vymazal², Aviran Itzhaki¹, Daniel Mordechovich¹,
Zoya Gurvich¹, Esther Shmueli¹, Dorit Goldsher^{3,4}, Yoram Wasserman¹ and
Yoram Palti^{1,4}

Address: ¹NovoCure Ltd, MATAM Advanced Technology Centre, Haifa 31905, Israel; ²Na Homolce Hospital, Roentgenova 2, Prague 5 150 30, Czech Republic; ³Rambam Medical Center, PO Box 9602, Haifa 31096, Israel and ⁴B. Rappaport Faculty of Medicine, Technion - Israel Institute of Technology, Technion City, Haifa 32000, Israel

E-mail: Eilon D Kirson* - eilon@novocure.com; Rosa S Schneiderman - rosa@novocure.com; Vladimír Dbalý - vladimir.dbalý@homolka.cz; František Továryš - frantisek.tovarys@homolka.cz; Josef Vymazal - josef.vymazal@homolka.cz; Aviran Itzhaki - aviran@novocure.com; Daniel Mordechovich - daniel@novocure.com; Zoya Gurvich - zoya@novocure.com; Esther Shmueli - eti@novocure.com; Dorit Goldsher - dgoldsher@rambam.health.gov.il; Yoram Wasserman - yoramw@novocure.com; Yoram Palti - yoram@novocure.com

* Corresponding author

Published 8 January 2009

Received 3 September 2008

BMC Medical Physics 2009, 9:1 doi:10.1186/1756-6649-9-1

Accepted 8 January 2009

This article is available from <http://www.biomedcentral.com/1756-6649/9/1>

© 2009 Kirson et al; licensee BioMed Central Ltd.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Background: The present study explores the efficacy and toxicity of combining a new, non-toxic, cancer treatment modality, termed Tumor Treating Fields (TTFields), with chemotherapeutic treatment in-vitro, in-vivo and in a pilot clinical trial.

Methods: Cell proliferation in culture was studied in human breast carcinoma (MDA-MB-231) and human glioma (U-118) cell lines, exposed to TTFields, paclitaxel, doxorubicin, cyclophosphamide and dacarbazine (DTIC) separately and in combinations. In addition, we studied the effects of combining chemotherapy with TTFields in an animal tumor model and in a pilot clinical trial in recurrent and newly diagnosed GBM patients.

Results: The efficacy of TTFields-chemotherapy combination in-vitro was found to be additive with a tendency towards synergism for all drugs and cell lines tested (combination index ≤ 1). The sensitivity to chemotherapeutic treatment was increased by 1–3 orders of magnitude by adjuvant TTFields therapy (dose reduction indexes 23 – 1316). Similar findings were seen in an animal tumor model. Finally, 20 GBM patients were treated with TTFields for a median duration of 1 year. No TTFields related systemic toxicity was observed in any of these patients, nor was an increase in Temozolomide toxicity seen in patients receiving combined treatment. In newly diagnosed GBM patients, combining TTFields with Temozolomide treatment led to a progression free survival of 155 weeks and overall survival of 39+ months.

Conclusion: These results indicate that combining chemotherapeutic cancer treatment with TTFields may increase chemotherapeutic efficacy and sensitivity without increasing treatment related toxicity.

ATTACHMENT 4

BMC Medical Physics 2009, 9:1

<http://www.biomedcentral.com/1756-6649/9/1>

Background

A new physical cancer treatment modality termed Tumor Treating Fields, or TFields, has recently been demonstrated to be highly effective when applied to cell cultures, animal cancer models, as well as to patients suffering from locally advanced and/or metastatic solid tumors [1-3]. In a pilot clinical trial, the medians of time to disease progression and overall survival of recurrent GBM patients treated by TFields alone were more than double the reported medians of historical control patients [1]. In contrast to the widely used physical treatment modality, ionizing radiation, TFields are not associated with significant side effects.

TFields are low intensity (1-2 V/cm), intermediate frequency (100 - 200 kHz) alternating electric fields generated by special insulated electrodes applied to the skin surface. These specially tuned fields have no effect on quiescent cells while having an anti-mitotic effect on dividing cells. During cytokinesis, TFields generate non-uniform intracellular fields that exert forces that move polar macromolecules and organelles towards the narrow neck, separating the newly forming daughter cells by a process termed dielectrophoresis. These molecular and organelle movements, together with an interference with the spindle tubulin polymerization process, inhibit cell division and lead to cell death [2]. Fortunately, the dividing cells of the hematopoietic system are not affected by TFields as the muscles surrounding the marrow containing bones serve as an effective electric field shield. Moreover, due to their relatively high frequency range and very low intensity, TFields do not stimulate nerves and muscles, do not generate meaningful temperature elevation or puncture the cell membrane (as the strong electroporation fields do [4]). Thus, TFields are not associated with meaningful toxicity in contrast to most anti-cancer agents currently in use [5].

In view of the unfavorable therapeutic indexes of the available effective chemical and physical (i.e. ionizing radiation) therapeutic agents, many cancer treatment protocols require simultaneous or sequential use of a number of therapeutic agents in an attempt to increase efficacy while maintaining tolerable toxicity [5-7]. Within this framework it is generally accepted that by adding ionizing radiation [8] to chemotherapy one gets both the benefit of the radiation effect as well as sensitization leading to an increased efficacy without a corresponding increase in toxicity. On the basis of the above this study explores the potential use of the new physical treatment modality TFields, in combination with chemotherapeutic agents in cell cultures, an animal tumor model as well as in patients with glioblastoma (GBM). As TFields are not associated with systemic toxicity [1] the expectations that their addition will result in an increase in efficacy alone

Methods

Cell cultures

Cells were cultured and maintained as previously described [1,2]. In brief Human breast cancer (MDA-MB-231) and human glioma (U-118) obtained from ATCC (USA) were cultured in DMEM + 10% FCS media in a 5% CO₂ incubator at 37°C. Drops consisting of 200 µl suspension of cells (100 × 10³ cells/ml) were placed at the centre of 35 mm Petri dishes, incubated for 2 hours to allow for cell attachment, then 1.5 ml of media were added and incubation was continued for an additional 22 h. Following this, the baseline cell count was estimated using the XTT colorimetric method (expressed as OD₀). The media in the Petri dishes was replaced by fresh media (3 ml), with or without a chemotherapeutic agent and incubated at a final temperature of 37° ± 0.5°C for 24 to 72 hours after which the cell number was re-estimated (OD_t). The relative number of viable cells at each time point following baseline was expressed as OD_t/OD₀ and treatment efficacy as the % change in proliferation relative to control:

$$(OD_t/OD_0)_{\text{experimental}} \cdot 100 / (OD_t/OD_0)_{\text{control}} \quad (1)$$

TFields treatment of cultures

As previously described [1,2], two pairs of electrodes, insulated by a high dielectric constant ceramic, were positioned normal to each other at a distance of 20 mm in treatment and control dishes. In the former, the electrodes were connected to sinusoidal waveform generator that generated fields of optimal frequencies in the medium [1,2,9]: 150 kHz for breast cancer and 200 kHz for glioma that changed direction by 90° every 250 ms. Field intensity was measured as described previously [2] and expressed as V/cm. For 72 h experiments the TFields intensity of 1.75 V/cm was used. For 24 h experiments 0.65, 1.25 and 1.75 V/cm TFields were used.

Four different sets of experiments were conducted in conjunction with each chemotherapeutic agent: untreated sham control, treatment with TFields, treatment with the chemotherapeutic agents, and combined TFields - Chemo treatment.

Assessment of combination Index and dose reduction index

The Chou and Talalay [10] method for assessing the combined effect of multiple drugs was used for the drug - TFields combinations. In order to assess whether the interactions between TFields and each of the chemotherapeutic agents is synergistic, additive or antagonistic combination indexes were calculated as follows. TFields intensity replaced the concentration (dose) variable in the analyses. Dose-response curves were generated for TFields and each drug to determine the median effect

ATTACHMENT 4

points. Variable ratios of drug concentrations to TTF fields intensities were used to calculate the Combination Index (CI) as follows:

$$CI = (C_{Drug(Combination)}^{X\% \text{ effect}} / C_{Drug(Alone)}^{X\% \text{ effect}}) + (I_{TTF(Combination)}^{X\% \text{ effect}} / I_{TTF(Alone)}^{X\% \text{ effect}}) \quad (2)$$

Where C are the drug concentrations and I the TTF fields intensities used to achieve a preset X% effect. Relationships of $CI < 1$ indicate more than additive – synergy, $CI = 1$ reflects additivity – summation and $CI > 1$ indicates less than additive or antagonism.

In order to assess whether TTF fields increase the sensitivity of tumor cells to various chemotherapeutic agents, the dose reduction index (DRI) of for each of these agents was calculated according to [11]. In short, the median-effect plots were for each chemotherapy-TTF fields combination, were constructed. The ratio of affected to unaffected number of cells (f_u/f_0) was plotted versus drug concentration on a log-log scale. The median effect point (D_m) was assessed by deriving the slope of the linear regression for each of the plots. The DRI for a 50% effect (DRI_m) was calculated as the ratio of D_m for drug alone and for combined drug-TTF fields.

$$DRI_m = D_{m(\text{drug alone})} / D_{m(\text{drug+TTF treatment})} \quad (3)$$

A DRI greater than 1 indicates an increase in sensitivity to the drug. The greater the DRI, the more significant the possible dose reduction.

In-vivo experiments

Combined TTF fields and Paclitaxel efficacy study in VX2 tumor bearing rabbits was conducted after approval by the NovoCure Internal Animal Care and Use Committee. All painful or anxiogenic procedures were performed under general anesthesia induced by intramuscular administration of 30 mg/kg of ketamine hydrochloride, 10 mg/kg xylazine hydrochloride and 1.5 mg/kg Acepromazine. The tumor tissue required for implantation was obtained from VX-2 tumor bearing carrier rabbits. The carrier rabbits had VX-2 tumors implanted intramuscularly in the thigh. When the tumor reached approximately 1 cm in diameter (about 3 weeks from implantation), the tumor was excised, minced in sterile saline and VX-2 tumor fragments obtained. Two fragments were injected using a large bore needle into the thigh muscles of both legs in a recipient rabbit for tumor propagation. For experimental animals, after laparotomy a fragment of tumor tissue (1 mm³) was implanted beneath the kidney capsule of the recipient rabbit.

The current experiment comprised 28 animals (7 in each of 4 groups). Fourteen days after tumor implantation the

initial tumor volume was assessed based on serial (2.2 mm interval) T1 weighted axial MRI images (1.5 Tesla, GE Genesis-Signa) obtained 3 minutes following IV injection of 3 ml of Gadolinium. Tumor volume was assessed from the area of the contrast enhancing lesion in each section. The animals were assigned randomly into 4 groups before treatment start.

1 TTF fields treated group. TTF fields were applied by using the NovoTTF-100A device (NovoCure LTD, Haifa, Israel). An optimal frequency of 150 kHz and intensity of 1–2 V/cm were used. TTF fields were switched sequentially between two perpendicular field directions.

2 Control group. Sham electrode heated to mimic heat generated by the TTF fields treatment (33–39 °C).

3 Paclitaxel (Medixel Injection, Icaro Pharmaceutical Industries LTD, Israel) treated group. 5 mg/animal diluted in 100 ml of normal saline were infused intravenously over a period of 30 minutes. Pre-medication was given subcutaneous 8 hours before and immediately prior to Paclitaxel administration (Dexamethasone (Dexavet-0.2 veterinary, VMD nv/s a Belgium) 0.5 mg/animal, Pramirine (Metoclopramide HCL, Rafa Laboratories LTD, Israel) 1 mg/animal, Diphenhydramine (10%, Medical M., Israel) 10 mg/animal).

4 Combined TTF fields and Paclitaxel treatment as above.

TTF fields were delivered to awake and behaving rabbits through four insulated electrode arrays placed circumferentially around the animal's abdomen, caudal to the rib-cage. The electrode insulation consisted of a high dielectric constant (>10,000) ceramic (PMN-PT) allowing efficient energy transfer through the insulation into the animal's body at the given frequencies. The electrodes were connected by a spiral cable to a swivel mechanism at the top of the cage, enabling the free movement. TTF fields were generated using the NovoTTF-100A system (NovoCure Ltd, Haifa, Israel). The animals were treated for 21 days continuously with MRI performed on days 14 and 21 for tumor volume assessment. The TTF fields intensity within the kidneys of the rabbits, using this electrode configuration, is between 1–3 V/cm (based on both finite element mesh simulations and direct measurements using an invasive probe – data not shown).

Pilot clinical trial

A single arm, pilot trial of the safety and efficacy of TTF fields treatment was performed in 20 patients with histologically proven glioblastoma multiforme (GBM) that met the inclusion/exclusion criteria specified in Supplemental Material Appendix A (briefly, KPS 70–100%, Age \geq 18). The trial was performed according to a protocol

ATTACHMENT 4

approved by the Na Homolce Institutional Review Board and the Czech Republic Ministry of Health. The patients were divided into two groups. The first group included 10 patients with recurrent GBM treated with TFields alone following failure of maintenance Temozolomide [1]. The second group consisted of 10 newly diagnosed patients who were at least 4 weeks post radiation therapy, who received TFields combined with maintenance Temozolomide. Prior to initiation of treatment, all patients underwent a baseline contrast MRI of the head, chest radiograph, EEG, ECG, complete blood & urine analyses, physical examination and neurological status. The patients were hospitalized for 1-3 days for observation and then released home where they received multiple 4-week courses of continuous NovoTTF-100A treatment until progression. The patients were seen once-month at an outpatient clinic where they underwent an examination similar to the initial one. TFields were applied to the patients using the NovoTTF-100A device set to deliver 200 kHz, 0.7 V/cm (RMS) fields (at the center of the brain) in 2 perpendicular directions, 1 second in each direction sequentially. The TFields were applied continuously using four insulated electrode arrays, each having a surface area of 22.5 cm², placed on opposing sides of the head with the tumor positioned directly between the electrode pairs [1]. As previously reported, to avoid electrolysis at the electrode surface and intracellular ion concentration changes that accompany long term current application, the electrodes were completely insulated by a ceramic having a very high dielectric constant (>10 000) that allowed the generation of the necessary electric fields [1,2]. Using this electrode configuration, the lowest TFields intensity at the center of the brain was 0.7 V/cm (RMS). This intensity was calculated using finite element mesh simulations and verified by direct measurement in large animals and a human volunteer [1].

The outcome endpoints of the study included safety, overall survival (OS) and progression free survival (PFS). Assessment of tumor response was based on monthly MRIs according to the Macdonald criteria [12]. Median OS and PFS were determined using Kaplan Meier curves [13]. In the first group, PFS in NovoTTF-100A treated patients was compared to a matched group of concurrent control patients who received salvage chemotherapy at recurrence (n = 18). PFS in Temozolomide/NovoTTF-100A treated patients was compared to the PFS of a

matched group of concurrent control patients (n = 32) who received Temozolomide alone (according to the protocol described by Stupp et al [14]). OS in both groups was compared to matched historical control data with the same Karnofsky performance score (>60) and age [14].

Results

Breast cancer cell cultures

Dose-response of culture exposure to TFields, paclitaxel, doxorubicin and cyclophosphamide, alone and in combination

The relationship between TFields intensity, at 150 kHz, and cell proliferation rate is given in Figure 1A. At the lowest field intensity of 0.63 V/cm there is no significant change in cell proliferation. For TFields intensities of 1.25, 1.75 and 2.95 V/cm cell proliferation decreases (control = 100%) to 90 ± 3%, 74 ± 4% and 25 ± 5%, respectively. The dose-response curves of cells exposed to paclitaxel, doxorubicin and cyclophosphamide, alone and in combination with 1.75 V/cm TFields for 72 hours, are given in Figures 1B, C & D. For each drug alone there is a decrease in cell proliferation with increase in concentration. For cyclophosphamide and doxorubicin complete inhibition of proliferation is achieved at high drug concentrations. For paclitaxel, the inhibitory effect of the drug saturates at about 300 nM, near the 13% level, indicating that a fraction of the cells are insensitive to the agent. Combined treatment with TFields and each of the chemotherapeutic agents caused a leftward shift of the dose response curves. This shift can be expressed as a decrease in the drug concentration leading to 50% inhibition of cell proliferation (IC₅₀ - Table 1).

Time course of the effects TFields, paclitaxel, doxorubicin and cyclophosphamide

Figure 2 displays the time course of proliferation inhibition during a continuous 72 hour exposure to TFields, paclitaxel, doxorubicin and cyclophosphamide alone and in combination with 1.75 V/cm TFields. It is seen that in all cases the inhibition during combined exposure is greater than for the chemotherapeutic agent alone. The differences between the separate and combined effects increase with time.

Recovery from treatment

Figure 3 demonstrates that a 24 hour exposure to individual chemotherapeutic agents induces a reduction of approximately 25% in viable cell number compared to

Table 1: IC₅₀ for chemotherapeutic drugs alone and in combination with 1.75 V/cm TFields after 72 hours of continuous treatment.

Chemotherapy	IC ₅₀ (drug alone)	IC ₅₀ (drug-TFields combination)
Paclitaxel	5.00 nM	0.005 nM
Doxorubicin	0.04 μM	0.002 μM
Cyclophosphamide	6.60 mM	0.044 mM

ATTACHMENT 4

BMC Medical Physics 2009 9 1

<http://www.biomedcentral.com/1756-6649/9/1>

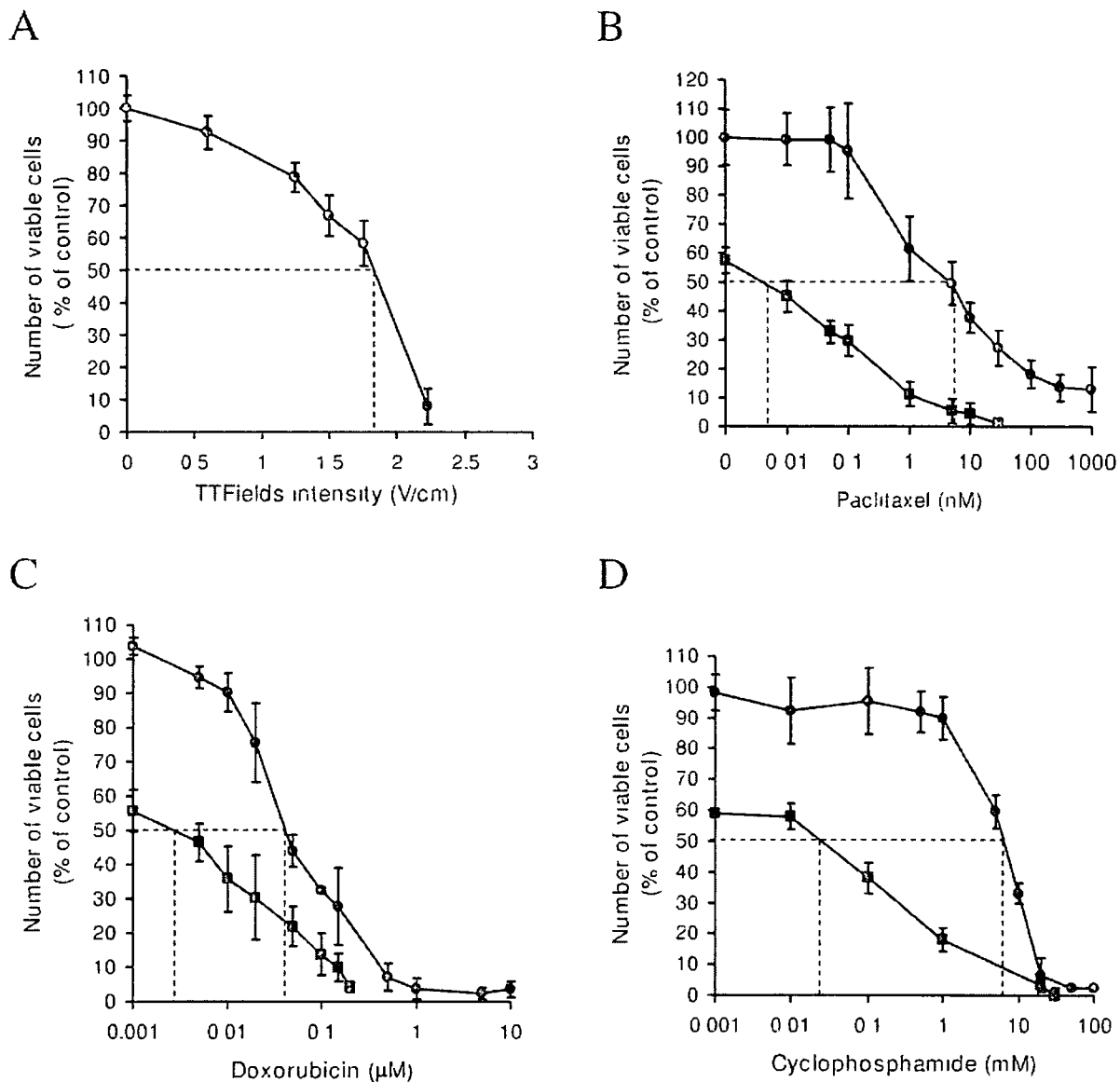


Figure 1

Effect of 72 hour continuous application of TTFIELDS and chemotherapeutic agents, separately and in combination on the cell proliferation of ER-negative MDA-MB-231 cells (presented as percent viable cells compared to control) (A) Percent viable cells vs TTFIELDS intensity Effect of different concentrations of paclitaxel (B), doxorubicin (C) and cyclophosphamide (D), alone and in combination with TTFIELDS of 1.75 V/cm In B, C and D Filled Circles – represent drug alone, Filled Squares – drug in combination with TTFIELDS Each point represents mean values \pm SEM of 18 to 36 replicate measurements. Dotted lines demarcate the IC₅₀ values for each curve

controls The proliferation rate (slope of the graph) recovers almost completely during the following 48 hours except for doxorubicin, where recovery is slower and

delayed by about 24 hours In contrast, addition of TTFIELDS to any one of these chemotherapeutic agents results in irreversible and complete inhibition of cell pro-

ATTACHMENT 4

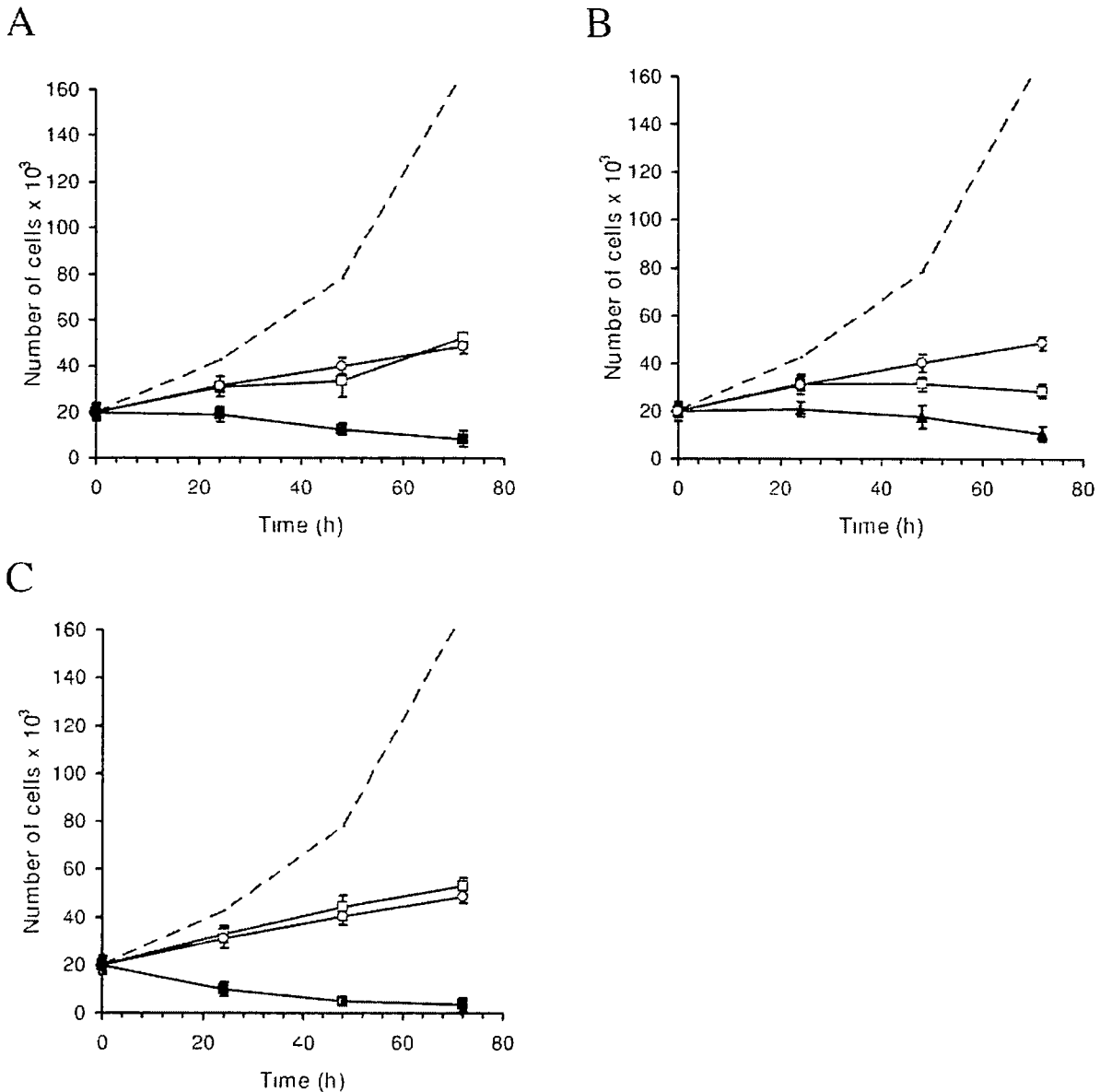


Figure 2
Time course of the effects of 72 hour exposure of MDA cells to Paclitaxel (A), Doxorubicin (B) and Cyclophosphamide (C) alone and in combination with 1.75 V/cm TTFields. Each graph shows the number of viable cells in culture over time in control cells (interrupted lines), drug alone (open squares), TTFields alone (open circles) and drug-TTFields combination (closed squares). Data are presented as mean \pm SEM. Each experimental condition included 18–36 samples.

liferation rate manifested as a decrease in the number of cells in culture. For Cyclophosphamide there is an almost complete loss of viable cells after 72 hours of combined treatment.

Glioma cell cultures

Combined effect of DTIC and TTFields in human glioma cell cultures
 In order to assess the combination between Temozolomide and TTFields in glioma cells, DTIC and TTFields

ATTACHMENT 4

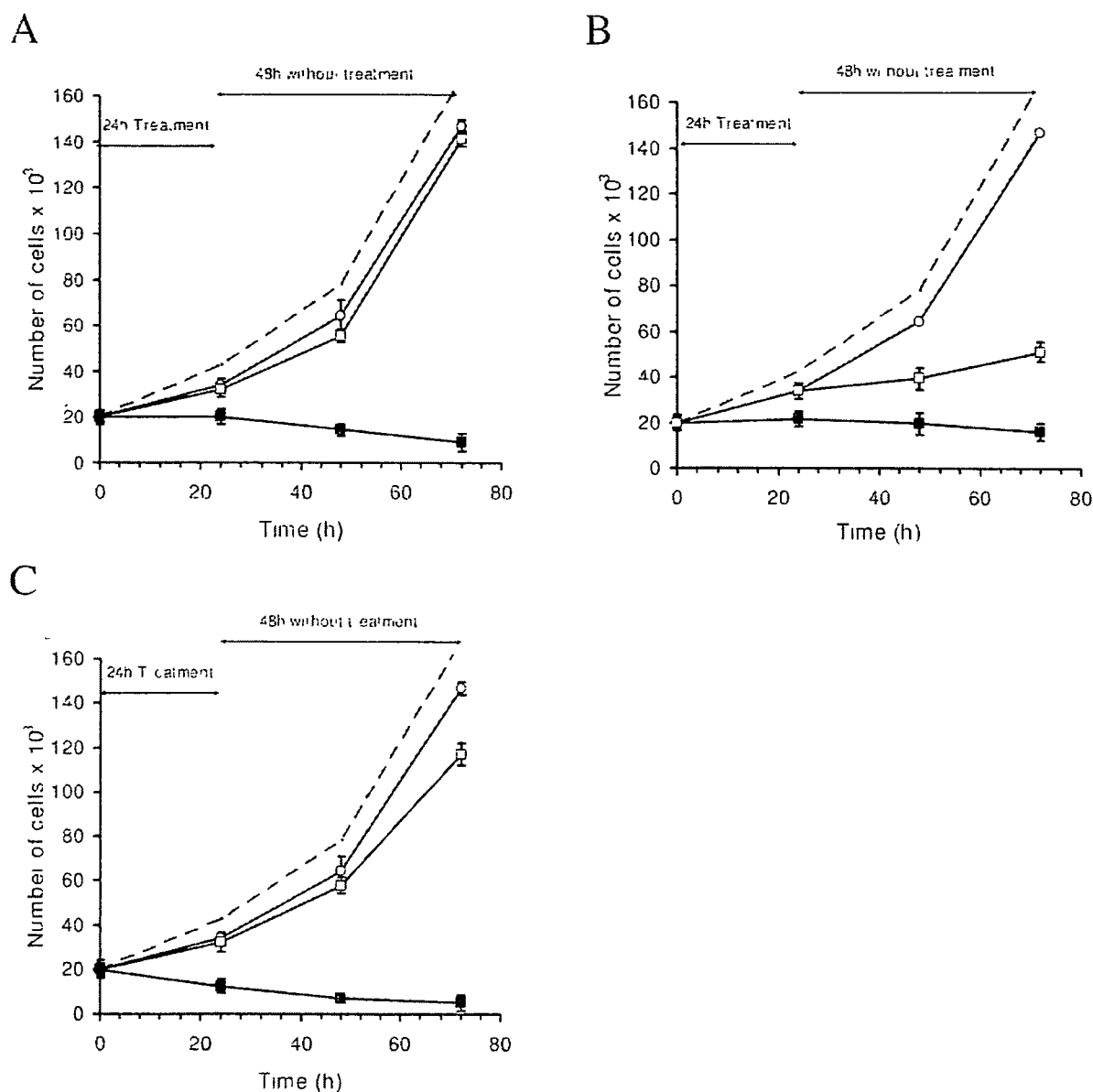


Figure 3

Time course of recovery from 24 hour exposure to Paclitaxel (A), Doxorubicin (B) and Cyclophosphamide (C) alone and in combination with 1.75 V/cm TFields Each graph shows the number of viable cells in culture over time in control cells (interrupted lines), drug alone (open squares), TFields alone (open circles) and drug-TFields combination (closed squares). Data are presented as mean \pm SEM. Each experimental condition included 18–36 samples.

were applied alone and in combination to U-118 cells in culture. Both DTIC and temozolomide act through a common degradation product (MTC). Thus light activated DTIC was used for these experiments as described

previously [15,16]. Figure 4 compares the DTIC dose-response curve with that obtained with DTIC - TFields combination. As we have shown in breast cancer cultures, the addition of TFields to a chemotherapeutic agent

ATTACHMENT 4

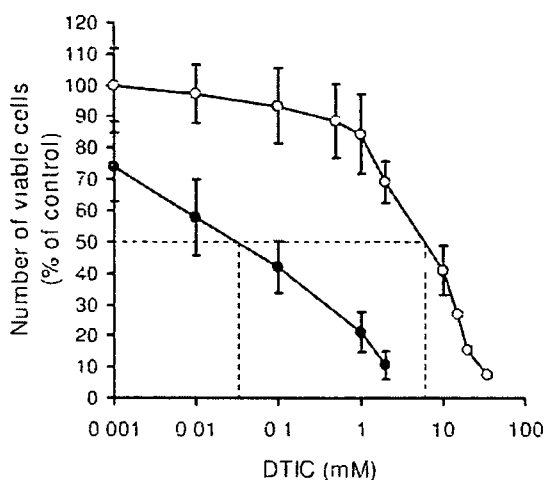


Figure 4
Effect of light activated DTIC and TTFIELDS (1.75 V/cm) on cell proliferation of U-118 glioma cells, presented as percent of viable cells compared to control. Open Circles – 72 hours of DTIC treatment alone. Filled Circles – 72 h of Combined DTIC – TTFIELDS treatment.

causes a leftward shift in the dose-response curve in glioma cells as well. The IC_{50} for DTIC alone in Figure 4 is 6.4 mM, whereas the IC_{50} for combined DTIC-TTFIELDS is two orders of magnitude lower (0.023 mM).

Analysis of combination efficacy and sensitivity in-vitro

Combination indexes

The mode of interaction between TTFIELDS and chemotherapeutic agents (synergism, additivity or antagonism) can be analyzed using Combination Indexes (CI) as described by [10,17]. In order to calculate the CIs for TTFIELDS-Chemotherapeutic agents, the extent of inhibition of cell growth was assessed after 24 hours of treatment with Paclitaxel, Doxorubicin and Cyclophosphamide alone or in combination with different intensities of TTFIELDS (0.625–1.75 V/cm, see Materials and Methods). Table 2 demonstrates that for breast cancer cells the CI for Doxorubicin is very close to 1, indicating additivity [10,11]. In contrast, for TTFIELDS with Paclitaxel and Cyclophosphamide the CIs are <1 indicating additivity with a tendency towards synergism.

Dose reduction indexes

In order to assess the extent of possible chemotherapeutic dose reduction when applied in combination with TTFIELDS, dose reduction indexes (DRI) for each drug-TTFIELDS combination were calculated based on the meth-

Table 2: Calculated Combination Indexes for human breast cancer (MDA-MB-231) cells treated with paclitaxel, doxorubicin or cyclophosphamide in combination with TTFIELDS.

TTFIELDS intensity (V/cm)	Combination index		
	MDA-MB-231 cells		
	Paclitaxel	Doxorubicin	Cyclophosphamide
	CI_{40}	CI_{50}	CI_{5c}
0.625	-	-	0.74
1.25	0.97	0.99	0.84
1.75	0.86	0.98	0.95

odology described by [11]. The DRIs for TTFIELDS-drug interaction after 72 hours of combined treatment was 1316 for paclitaxel, 23 for doxorubicin, 152 for cyclophosphamide and 175 for DTIC (in U-118 glioma cells). Thus a significantly reduced dose (1–3 orders of magnitude lower drug concentration) may be used in combination with TTFIELDS to achieve the same level of efficacy.

Effect of combined paclitaxel and TTFIELDS on VX2 tumors in rabbits

Prior to testing the combined efficacy of paclitaxel and TTFIELDS on VX2 tumors implanted within the kidneys of rabbits, the dose-response of paclitaxel in this animal tumor model was determined. A dose of Paclitaxel leading consistently to a 15–20% inhibition in tumor growth (5 mg/rabbit) was chosen for subsequent combination experiments with TTFIELDS.

As seen in Figure 5, untreated tumors increased in volume by a factor of 70 from baseline. Paclitaxel treated tumors grew by a factor of 58 from baseline. TTFIELDS treated tumors grew by a factor of 34 from baseline and tumors treated by TTFIELDS-Paclitaxel combination grew by a factor of 22 from baseline. Thus the TTFIELDS-Paclitaxel combination treatment inhibited tumor growth by 69% compared to the growth of control tumors, while Paclitaxel alone inhibited tumor growth by 15% compared to the growth of control tumors and TTFIELDS alone by 53% compared to the growth of control tumors. Thus, additivity was seen between TTFIELDS and Paclitaxel at the intensity and concentration used. Differences between curves were statistically significant ($p < 0.01$, ANOVA).

Pilot clinical trial in GBM patients

Twenty patients with histological diagnosis of GBM were treated continuously for an average of 1 year (range 2.5–24 months). Ten recurrent GBM patients were treated with TTFIELDS alone as salvage therapy. Ten newly diagnosed

ATTACHMENT 4

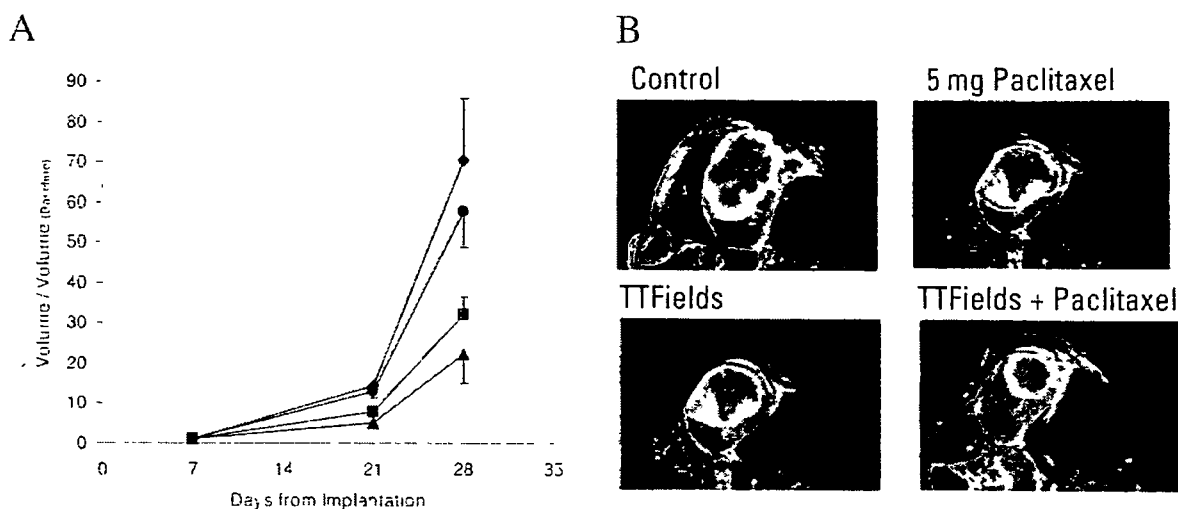


Figure 5
Effect of combined Paclitaxel/TTFields on VX2 tumors in Rabbits A VX-2 Kidney tumor volumes were normalized to pre-treatment tumor volume (day 7) and are presented over time for: control (diamonds), 5 mg Paclitaxel (circles), TTFields (squares) and combined TTFields-Paclitaxel (triangles) The effect of combined TTFields and Paclitaxel is equal to the sum of the effects of either treatment alone at both time points measured during the study (2 and 3 weeks from treatment start, n = 23, bars are standard errors of means) B Exemplary MRIs of the maximal contrast enhancing tumor area (demarcated by orange borders) in the kidneys of rabbits in each of the experimental groups (sham control, Paclitaxel 5 mg, TTFields 2 V/cm, combined Paclitaxel and TTFields)

GBM patients, that had undergone surgery and thereafter received radiation therapy with adjuvant Temozolomide, were treated with the combination of TTFields in parallel to maintenance Temozolomide [14]. In both groups of patients no device related serious adverse effects were observed. The only device related toxicity reported was a dermatitis which appeared most often (18 of 20 patients) during the second month of treatment. The severity of the dermatitis decreased upon use of topical corticosteroids and periodic electrode relocation. The dermatitis continued for the duration of treatment and resolved completely within days to weeks from treatment termination.

In the second group, no increase in Temozolomide related adverse events was seen due to the combination with TTFields (see Table 3).

As reported previously [1], both progression free survival (PFS) and overall survival (OS) in the recurrent GBM salvage therapy group were at least double that of concurrent and historical controls, respectively. The efficacy of the TTFields-Temozolomide combination in the second group of patients was assessed using Kaplan-Meier curves [13] of PFS and OS. The Kaplan-Meier curves for the PFS of these patients, treated by combined TTFields - Temozolomide are shown in Figure 6A. The median PFS of the

combination treated patients is 155 weeks versus 31 weeks for concurrent controls treated with maintenance Temozolomide alone. Note that 5 of 10 patients are currently progression free. Figure 6B compares the OS of the patients that received the combination treatment (Red line) with a matched historical control (KPS > 60, Median age 54) (Black line [14]). It is seen that for the TTFields - Temozolomide combination treated patients, the Median OS > 39 months versus about 14.7 months for matched historical control patients who received maintenance Temozolomide alone. It should be noted that at the time

Table 3: Toxicities by grade and causality in the newly diagnosed GBM patients treated with combined TTFields-Temozolomide.

	Grade		Causality assessment
	I-II	III-IV	
Elevated LFTs	6/10	0/10	Anti-Epileptic Drugs
Hyperglycemia	4/10	0/10	Oral Steroids
Anemia	6/10	0/10	Temozolomide
Thrombocytopenia	2/10	0/10	Temozolomide
Leucopenia	3/10	0/10	Temozolomide
Headache	2/10	0/10	Underlying disease
Seizures	1/10	0/10	Underlying disease
Dermatitis	10/10	0/10	NovoTTF-100A

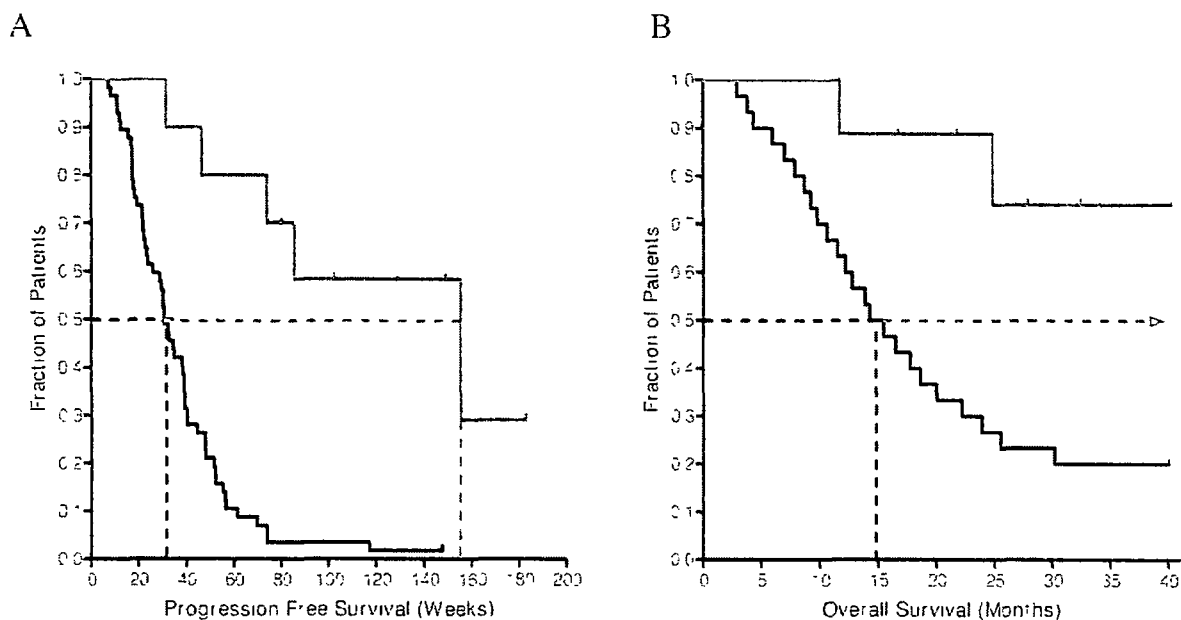


Figure 6
Kaplan Meier curves for **A** – progression free survival (PFS) and **B** – overall survival (OS) of newly diagnosed GBM patients receiving either combined TFields – Temozolomide treatment or Temozolomide treatment alone. Red line – patients receiving combined TFields – Temozolomide treatment ($n = 10$). Black line – concurrent/historical control patients that received Temozolomide treatment alone. **A** – The difference between the PFS curves is highly significant – Log-Rank Test ($P = 0.0002$), Hazard Ratio 3.32 (95%CI 1.9–5.9). **B** – The difference between the OS curves is highly significant – (Log-Rank Test, $P = 0.0018$). Dashed lines mark the median values for each curve.

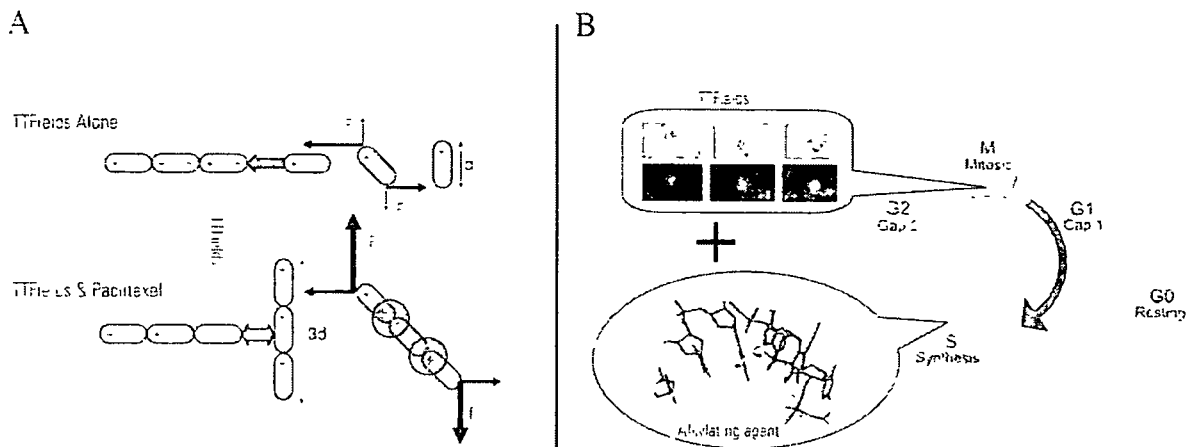
of this report 8 of 10 patients receiving the TFields-Temozolomide combination treatment, are alive.

Discussion

Cancer treatment with drug combinations was introduced in order to improve therapeutic indexes through dose reduction of each drug and increase treatment efficacy. In this study the exposure of cancer cells to combined chemotherapy and TFields was studied in cell cultures, an animal tumor model and in a pilot clinical trial in recurrent and newly diagnosed GBM patients. The results of this study support the possibility that TFields may be used, not only as an effective stand alone anti-proliferation agent (as shown previously in [1]), but also as an effective adjuvant that enhances chemotherapy efficacy without an increase in toxicity. In addition to this increase in efficacy, these results raise the possibility of dose reduction of chemotherapy when used in combination with TFields. This is of utmost importance since, at tolerable doses the efficacy of available cancer therapeutic agents is often far from optimum while being associated with a high degree of toxicity.

With regards to the mechanisms involved, one may assume that tumor cells are sensitized to TFields by chemotherapy, much like another well established physical therapy – ionizing radiation [8,18,19]. In the specific case of Paclitaxel, one of the most commonly used treatments for late-stage human breast cancer [20], the combined effect may be attributed to their similar site of action – the spindle microtubules [1,2,21]. Taxanes act by stabilizing the link between individual tubulin dimers [21]. As illustrated schematically in Figure 7A taxanes increase the length of tubulin filaments within the cell. One of the mechanisms of action of TFields is the misalignment of mitotic spindle filaments as a result of TFields forces on tubulin chains [2]. The increase in filament length due to taxanes, increases the dipole moment of these macromolecules, leading to an increase in the TFields induced forces and thus to a higher sensitivity of the cell to TFields (see Figure 7A).

Doxorubicin that has a broad spectrum of activity both in experimental tumor models and in human malignancy, affects both DNA and RNA synthesis [22]. Cyclophosphamide (an alkylating agent) inhibits DNA replication by

**Figure 7**

Mechanisms of potentiation of chemotherapeutic efficacy by TTFIELDS A Tubulin chains are elongated by Paclitaxel, leading to an increase in the average dipole moment of free tubulin chains (d – length of an individual tubulin dimer, f – force between the microtubule chain and the dimer, F -force acting on the tubulin dimmers by TTFIELDS: Arrow length is proportional to the intensity of these forces) The forces TTFIELDS exert on these larger dipoles, F , are enhanced leading to an increase in the disruption of the mitotic spindle by TTFIELDS B TTFIELDS act as an M-phase inhibitor, while alkylating agents act at the G and S phases of the cell cycle This separation between cell cycle phases affected explains the additivity seen experimentally

interfering with the separation of the double stranded DNA essential for transcription [23]. As illustrated in Figure 7B, since TTFIELDS act at a completely different stage (M phase) of the cell cycle from both these agents, additivity between chemotherapy and TTFIELDS can be expected.

Since the data for newly diagnosed GBM patients, which points to well over a 300% increase in PFS and OS, was obtained only with combination treatment, one cannot directly separate the TTFIELDS effects from the chemotherapeutic effect. However, if we assume that the TTFIELDS therapeutic efficacy for newly diagnosed patients is similar to recurrent GBM, i.e. the median of OS is increased by 270% [1] while the published Temozolomide data indicates an increase of about 20% in OS compared to ionizing radiation treatment alone [14], the results presented in figure 6 point towards additivity between TTFIELDS and Temozolomide. It is important to note that this significant increase in efficacy was obtained without any increase in device or drug related toxicity (see table 3).

An additional important finding is that both 24 h and 72 h combination treatments *in-vitro* result in severe irreversible cellular damage in contrast to chemotherapy alone. This result strengthens the assumption that combination therapy with TTFIELDS may be much more effective than treatment by individual agents.

Conclusion

The results of the present study support the notion that TTFIELDS may be used clinically not only as an anti-proliferation agent as shown before [1] but also as effective sensitizers of currently used chemotherapeutic agents. Such sensitization was not shown to be associated with any additional systemic toxicity. Moreover, as demonstrated by the high DRIs calculated in this study, chemo/TTFIELDS combinations are expected to provide the same or even greater therapeutic efficacy with much lower drug concentrations thus lowering further the overall toxicity.

Competing interests

LK, RSS, AI, DM, ZG, ES and YW are employees of NovoCure Ltd.

YP has a minority holding in NovoCure Ltd.

VD, FT, IV and DG have no competing interests.

Authors' contributions

FK – planned the pre-clinical and clinical experiments, supervised their execution analyzed results and wrote parts of the manuscript. RSS and IT – Performed the *in-vitro* experiment and assisted in the *in-vivo* experiments. DM, ZG and AI – Performed the *in-vivo* experiments. DG – Performed the MRI imaging for the *in-vivo* experiments. YW – Planned the medical devices and treatment parameters.

ATTACHMENT 4

BMC Medical Physics 2009, 9:1

<http://www.biomedcentral.com/1756-6649/9/1>

ters for all experiments. VD, FT and JV – performed the clinical trial in GBM patients (clinical investigators). YP – invented the concept of TFields, helped interpret all results and wrote the majority of the manuscript.

Appendix

Appendix A – Eligibility criteria for the pilot GBM trial

Inclusion criteria:

Histologically proven diagnosis of GBM

Age over 18 years.

Karnofsky scale ≥ 70

Participants of child bearing age had to be receiving efficient contraception

Willing and able to sign an informed consent prior to participation in the study

Exclusion criteria:

Patients actively participating in another clinical trial

Patients who received any anti-tumor therapy in the four weeks prior to trial initiation (steroids are permitted, however, the dose must be stable or decreasing during the trial).

Patients suspected of suffering from radiation necrosis (according to a PET scan).

Pregnancy

Patients with one of the following co-morbidities

Patients with an implanted pacemaker or documented arrhythmias

Significant renal, hepatic or hematologic disease

Significant additional neurological disorder

Seizure disorder unrelated to the patient's tumor

Pre-existing dementia

Progressive degenerative neurological disorder

Meningitis or encephalitis

Hydrocephalus associated with increased intracranial pressure (ICP)

Acknowledgements

We wish to thank Mr. Michael Parkanski and Mrs. Orly Azrad for providing technical support and study coordination for the clinical study. Both MP and OA are employees of NovoCure Ltd. EK, RSS, AI, DM, ZG, ES and YW are employees of NovoCure Ltd. VD, FT and JV performed the clinical trial which was sponsored by NovoCure Ltd.

References

- 1 Kirson ED, Dbaly V, Tovaryš F, Vymazal J, Soustiel JF, Itzhaki A, Mordechovich D, Steinberg-Shapira S, Gurvich Z, Schneiderman R, Wasserman Y, Salzberg M, Ryffel B, Goldsher D, Dekel E, Palti Y. **Alternating electric fields arrest cell proliferation in animal tumor models and human brain tumors.** *Proc Natl Acad Sci USA* 2007, **104**(24):10152-10157.
- 2 Kirson ED, Gurvich Z, Schneiderman R, Dekel E, Itzhaki A, Wasserman Y, Schatzberger R, Palti Y. **Disruption of cancer cell replication by alternating electric fields.** *Cancer Res* 2004, **64**(9):3288-3295.
- 3 Salzberg M, Kirson E, Palti Y, Rochlitz C. **A pilot study with very low-intensity, intermediate-frequency electric fields in patients with locally advanced and/or metastatic solid tumors.** *Onkologie* 2008, **31**(7):352-365.
- 4 Heller R, Gilbert R, Jaroszeski MJ. **Electrochemotherapy: an emerging drug delivery method for the treatment of cancer.** *Adv Drug Deliv Rev* 1997, **26**(2-3):185-197.
- 5 Bantinas R, Hohl R, Peterson D. **Management of Drug Toxicity.** In *The Chemotherapy Source Book* 3rd edition. Edited by Perry MC. Lippincott Williams & Wilkins, 2001:399-559.
- 6 Bryer M. **Combined Modality Therapy.** In *The Chemotherapy Source Book* 3rd edition. Edited by Perry MC. Lippincott Williams & Wilkins, 2001:73-81.
- 7 Burris H. **Combination Chemotherapy.** In *The Chemotherapy Source Book* 3rd edition. Edited by Perry MC. Lippincott Williams & Wilkins, 2001:69-73.
- 8 Leonard CE, Chan DC, Chou TC, Kumar R, Bunn PA. **Paclitaxel enhances in vitro radiosensitivity of squamous carcinoma cell lines of the head and neck.** *Cancer Res* 1996, **56**(22):5198-5204.
- 9 Kirson ED, Dbaly V, Rochlitz C, Tovaryš F, Salzberg M, Palti Y. **Treatment of locally advanced solid tumors using alternating electric fields (TFields) – a translational study.** *Proceedings of 97th AACR Annual Meeting 2006, Washington, DC 2006*.
10. Chou TC, Talalay P. **Quantitative analysis of dose-effect relationships: the combined effects of multiple drugs or enzyme inhibitors.** *Adv Enzyme Regul* 1984, **22**:27-55.
- 11 Chou TC. **Theoretical basis, experimental design, and computerized simulation of synergism and antagonism in drug combination studies.** *Pharmacol Rev* 2006, **58**(3):621-681.
- 12 Macdonald DR, Cascino TL, Schold SC Jr. **Cairncross JG. Response criteria for phase II studies of supratentorial malignant glioma.** *J Clin Oncol* 1990, **8**(7):1277-1280.
- 13 Jager KJ, van Dijk PC, Zoccali C, Dekker FW. **The analysis of survival data: The Kaplan-Meier method.** *Kidney Int* 2008.
- 14 Scapp R, Mason WP, Bent MJ van den, Veller M, Fisher B, Taphoorn MJ, Belanger K, Brandes AA, Marosi C, Bogdahn U, Curschmann J, Janzer RC, Ludwin SK, Gorlia T, Allgeier A, Lacombe D, Cairncross JG, Eisenhauer E, Mirmanoff RO. **Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma.** *N Engl J Med* 2005, **352**(10):987-996.
- 15 Lev DC, Ruiz M, Mills L, McGary EC, Price JE, Bar-Eli M. **Dacarbazine causes transcriptional up-regulation of interleukin 8 and vascular endothelial growth factor in melanoma cells: a possible escape mechanism from chemotherapy.** *Mol Cancer Ther* 2003, **2**(8):753-763.
- 16 Shibuya H, Kato Y, Saito M, Isobe T, Tsubota R, Koga M, Toyota H, Mizuguchi J. **Induction of apoptosis and/or necrosis following exposure to antitumor agents in a melanoma cell line, probably through modulation of Bcl-2 family proteins.** *Melanoma Res* 2003, **13**(5):457-464.
- 17 Steel GG, Peckham MJ. **Exploitable mechanisms in combined radiotherapy-chemotherapy: the concept of additivity.** *Int J Radiat Oncol Biol Phys* 1979, **5**(1):85-91.

ATTACHMENT 4

BMC Medical Physics 2009, 9:1

<http://www.biomedcentral.com/1756-6649/9/1>

- 18 Novello S, Le Chevalier T Use of chemo-radiotherapy in locally advanced non-small cell lung cancer. *Eur J Cancer* 2002, **38(2)**:292-299
- 19 Choy H, Kim DW Chemotherapy and irradiation interaction. *Semin Oncol* 2003 **30(4 Suppl 9)** 3-10
- 20 Rowinsky EK, Donehower RC Paclitaxel (taxol). *N Engl J Med* 1995, **332(15)**:1004-1014
- 21 Abal M, Andreu JM, Barasoain I Taxanes: microtubule and centrosome targets, and cell cycle dependent mechanisms of action. *Curr Cancer Drug Targets* 2003, **3(3)**:193-203
- 22 Plosker GL, Faulds D Epirubicin A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in cancer chemotherapy. *Drugs* 1993 **45(5)**:788-856
- 23 Sladek NE Influence of aldehyde dehydrogenase activity on the sensitivity of lymphocytes and other blood cells to oxazaphosphorines. *Methods Find Exp Clin Pharmacol* 1987, **9(9)**:617-626

Pre-publication history

The pre-publication history for this paper can be accessed here

<http://www.biomedcentral.com/1756-6649/9/1/prepub>

Publish with **BioMed Central** and every scientist can read your work free of charge

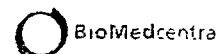
"BioMed Central will be the most significant development for disseminating the results of biomedical research in our lifetime"

Sir Paul Nurse, Cancer Research UK

Your research papers will be

- available free of charge to the entire biomedical community
- peer reviewed and published immediately upon acceptance
- cited in PubMed and archived on PubMed Central
- yours — you keep the copyright

Submit your manuscript here
http://www.biomedcentral.com/info/publishing_adv.asp



ATTACHMENT 5

EF-14 Participating Centers

Steering committee: Dr. Roger Stupp – CHUV Lausanne

Dr. Phil Gutin – MSKCC, NY

Dr. Eric Wong – Beth Israel, Boston (also a site)

Dr. Herbert Engelhard – UIC, Chicago (also a site)

Dr. Robert Weil – CCF, Cleveland (also a site)

Prof. Manfred Westphal – Uniklinikum, Hamburg (also a site)

US: UPMC – Dr. Lieberman Geisinger – Dr. Toms

Weill Cornell – Dr. Pannullo Tufts – Dr. Zhu

Baylor – Dr. Fink

MD Anderson Orlando – Dr. Avgeropoulos

USC – Dr. Chen

Maine Medical Center – Dr. Desai

UCSD – Dr. Read

NJ Neuroscience – Dr. Landolfi

Europe & Israel: University Hospital Kiel – Prof. Mehdorn PSP Paris – Dr. Taillibert

Tel Aviv Medical Center – Dr. Kanner Chu Lyon – Prof. Honnorat

Univ. Hospital, Milano – Dr. Bello

Univ. Graz – Prof. Payer

Besta Institute, Milano – Dr. Salmaggi

Hospital Purpan – Dr. Benouaich

NOROCURE

- If you are filing for an **Additional (Not Automatic) 3-Month Extension**, complete only Part II and check this box **X**
- Note.** Only complete Part II if you have already been granted an automatic 3-month extension on a previously filed Form 8868.
- If you are filing for an **Automatic 3-Month Extension**, complete only Part I (on page 1).

Part II Additional (Not Automatic) 3-Month Extension of Time. Only file the original (no copies needed).

Type or print File by the extended due date for filing the return. See instructions.	Name of Exempt Organization THE NOTSEW ORM SANDS FOUNDATION	Employer identification number 76-0455176
	Number, street, and room or suite no. If a P.O. box, see instructions. 2470 S. DAIRY ASHFORD	For IRS use only
	City, town or post office, state, and ZIP code. For a foreign address, see instructions. HOUSTON, TX 77077	

Check type of return to be filed (File a separate application for each return):

<input type="checkbox"/> Form 990	<input checked="" type="checkbox"/> Form 990-PF	<input type="checkbox"/> Form 1041-A	<input type="checkbox"/> Form 6069
<input type="checkbox"/> Form 990-BL	<input type="checkbox"/> Form 990-T (sec. 401(a) or 408(a) tr ust)	<input type="checkbox"/> Form 4720	<input type="checkbox"/> Form 8870
<input type="checkbox"/> Form 990-EZ	<input type="checkbox"/> Form 990-T (trust other than above)	<input type="checkbox"/> Form 5227	

STOP! Do not complete Part II if you were not already granted an automatic 3-month extension on a previously filed Form 8868.

- The books are in the care of **BKD, LLP**
Telephone No. **210 341 9400** FAX No. _____
- If the organization does not have an office or place of business in the United States, check this box
- If this is for a Group Return, enter the organization's four digit Group Exemption Number (GEN) _____. If this is for the whole group, check this box . If it is for part of the group, check this box and attach a list with the names and EINs of all members the extension is for.

4 I request an additional 3-month extension of time until 11/15/2010

5 For calendar year 2009, or other tax year beginning _____ and ending _____


6 If this tax year is for less than 12 months, check reason. Initial return Final return Change in accounting period

7 State in detail why you need the extension
ADDITIONAL TIME IS REQUIRED TO ACCUMULATE THE INFORMATION NECESSARY TO FILE A COMPLETE AND ACCURATE RETURN.

8a If this application is for Form 990-BL, 990-PF, 990-T, 4720, or 6069, enter the tentative tax, less any nonrefundable credits See instructions.	8a \$
b If this application is for Form 990-PF, 990-T, 4720, or 6069, enter any refundable credits and estimated tax payments made Include any prior year overpayment allowed as a credit and any amount paid previously with Form 8868.	8b \$
c Balance Due. Subtract line 8b from line 8a. Include your payment with this form, or, if required, deposit with FTD coupon or, if required, by using EFTPS(Electronic Federal Tax Payment System). See instructions.	8c \$

Signature and Verification

Under penalties of perjury, I declare that I have examined this form, including accompanying schedules and statements, and to the best of my knowledge and belief, it is true, correct, and complete, and that I am authorized to prepare this form.

Signature  Title CPA Date 8/3/10

BKD, LLP
10001 REUNION PLACE, SUITE 400
SAN ANTONIO, TX 78216-4137