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Nanomedicine in Cancer Treatment

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Introduction

More than half of the populations over 65 years old suffer from a cancer disease. Tumor research, therefore, also seeks new and more efficient forms of therapy.

Since cytostatics have harmful effect on all cells in the human body, the concept of magnetic drug targeting offers an interesting alternative to conventional tumor therapy [1]. The concept has been described in the literature and tested on animal models. The intravasal availability of the ferrofluids and the magnetic sensitivity were critical. The particles must be large enough to be attracted by a magnetic field, and to migrate into the tumor in this way, in order to release their active substance there [2].

Materials and Methods

Animal studies

A magnetic field strength of 0.6 tesla was applied externally to the body [3]. Iron oxides [Fe_3O_4] were administered intravasally into a vein or artery (Figure 1). Cytostatics were bonded to the iron oxides [Fe_3O_4]. The animal studies were conducted with sarcomas such as rhabdomyosarcoma (Tables 1 and 2).

Results: It was demonstrated that mitoxantrone has a higher concentration in the tumor than the mitoxantrone concentration [2], in the peripheral blood (Table 3).

The results revealed that iron bonded cytostatics contributed towards a reduction in the volume of the tumor and encouraged for further experimental surgical studies (Table 4).

Human study

70-year old female patient with metastases mammary carcinoma on left, initial diagnosis in May 2008, has been detected. Further diagnosis was arterial hypertension and obesity (97 kg, 161 cm).

Results: The CT showed an exulcerated timorous mass approx. 10 cm

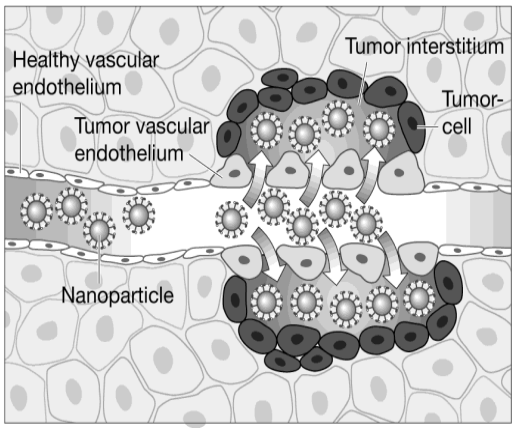

Figure 1: Extravasation of the nanoparticles in the tumor tissue.

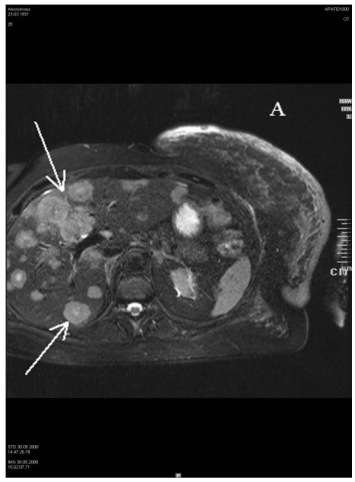

Figure 2: 30.05.2008 metastasis of liver prior to treatment–arrow marks metastasis in the upper and lower liver, small node as the size of 14.9 cm^3.

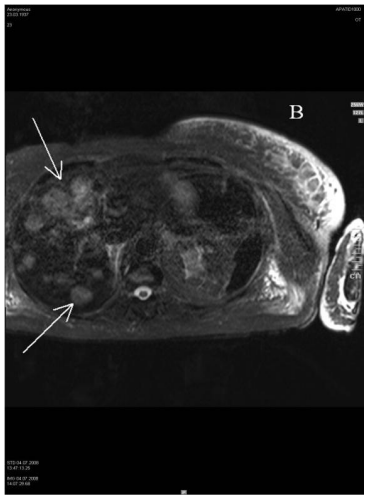

Figure 3: 04.07.2008 four weeks after treatment, reduction of all metastasis in the liver visible–more metastasis in right lobe shrank of 45% volume, to 8.0 cm^3.

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Group	Operative measure	Duration*	Number of animals
I	1 mg/kg BW MagnaDrug mitoxantrone** in a magnetic field	Once on one day 30 min	6
II	1 mg/kg BW MagnaDrug mitoxantrone** without a magnet	30 min	6
III	1mg/kgBW mitoxantrone** without a magnetic field	30 min	6
IV	1 mg/kg BW MagnaDrug mitoxantrone**	1st day 30 min 2nd day 30 min	6
V	1 mg/kg BW MagnaDrug mitoxantrone** without a magnet	1st day 30 min	6
VI	1mg/kg BW mitoxantrone** without a magnetic field	1st day 30 min	6

*Duration: Duration of exposure to the magnetic field
** Slow intravenous injection over 5 minutes
Total number=Σ 36

Table 1: Study groups in the biodistribution.

Target value	Parameter
General condition	survival, reflex status, weight
Biodistribution of iron	blood, tumor, liver

Table 2: Target values and parameters investigated.

	Group I	Group II	Group III	Group IV	Group V
Group I	o/o	o/o	o/o	o/o	o/o
Group II	0.6190	o/o	o/o	o/o	o/o
Group III	0.0173*	0.0087**	o/o	o/o	o/o
Group IV	0.2403	0.2403	0.0087**	o/o	o/o
Group V	0.0952	0.0238*	0.0357*	0.9048	o/o
Group VI	0.1775	0.1775	0.0079**	0.9307	0.5714

* Significant p values
** Highly significant p values

Table 3: p values for comparison of the mitoxantrone concentration in the tumor between Groups I - VI.

Patient L.K.	Unit	Day -2	Day 0	Day 1	Day 2	Day 3	Day 4	After 2 weeks
Iron	µg/dl	131	44	46	96	117	151	119
Ferritin	ng/ml	185.7	305.1	366.8	535.4	729.5	1011.0	1985.0

Table 4: Iron oxide and ferritin on day -2, 0, 1, 2, 3 and 4 and after 2 weeks.

Sample designation		Sample 1	Sample 2
Matrix		blood	tumor tissue directly under the magnet
Parameter	**unit**	**content**	**content**
Microwave pressure break-down HNO_3/H_2O_2		X	X
Iron, tot. (Fe)	µg/dl	151	440

Table 5: Blood sampling on the 4th day.

in diameter in the region of the left breast (500 ml), Table 5 shows the pathologically changed axillary lymph nodes of maximum 2.5 cm diameter and multiple metastases of maximum 5 cm diameter, in both lobes of the liver (Figure 2).

The volume of the smaller liver metastasis, identified with an arrow in the right lobe, has decreased from approx. 14.9 cm^3 to approx. 8.0 cm^3, *i.e.* by approx. 45% and until 25.03.2009 to 90% (Figure 3).

The exulceration at the breast stopped, so that an imputation of the breast had been successfully performed in 11/2008. The patient has responded well to the therapy. Her physical and mental condition is good and well tolerated, she felt well, and no complications or side effects occurred in the patient.

Conclusion

The animal study shows in the living organism, an effect of the magnetic field, concentrating on the iron particles. The case study on a human shows a reversible granulocytopenia, neither gastritis, nor alopecia or stomatitis. The data show partial metastatic reduction as per literature. Further patients were treated with the same dose; long-term results are being investigated. This therapy method is a possible option with relatively few side effects.

References

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