A comparison of caliper measurements to direct optical 3D tumor volume determination

Introduction

Vernier caliper measurements are commonly used to monitor tumor growth during pre-clinical oncology studies in mice. In this method, width and length are measured and a tumor volume formula is used to calculate the tumor volume. Usually, changes in tumor height are not taken into consideration. The following document will compare and reference such caliper measurements to an innovative direct 3D method in which an advanced optical method of 3D imaging is used to image the tumors and monitor tumor volume growth. The TM900, previously from Peira, since 2023 incorporated in Budetec, is such an instrument. We are also evaluating how both methods compared to the actual tumor volume.

Materials and Methods

For this evaluation three different comparison tests were done;

1. **Plasticine tumor simulations:** Using plasticine, a sphere, boll, was created by hand. Its diameter was measured by a vernier caliper, and its volume calculated. From this amount, different, randomly molded, by hand, tumor shapes were created. The volumes of these shapes were measured by the Budetec TM900v2, the newer version of the instrument. The TM900v2 also determines tumor width and length, so a virtual caliper measurement. The volume was also calculated by inputting those in the tumor volume formula. This was done for a small, medium and big volume.
2. **Subcutaneous and extracted tumor**: From 3 mice with different stages of tumor growth, small, medium and big, tumor sizes were measured using the Piera TM900. Also here, using the TM900 output tumor widths and lengths, so a virtual caliper measurement, the volume was also calculated by using the tumor volume formula. The tumors were then extracted, and the separated tumor was measured by the TM900.
3. **During a study, formula calculations vs TM900v2:** For 4 animals during a study, the volume was monitored by the TM900v2. The growth evolution is then compared to what is generated by the tumor volume formula.

“Mushroom” effect in 3D scanner measurements on spherical shapes

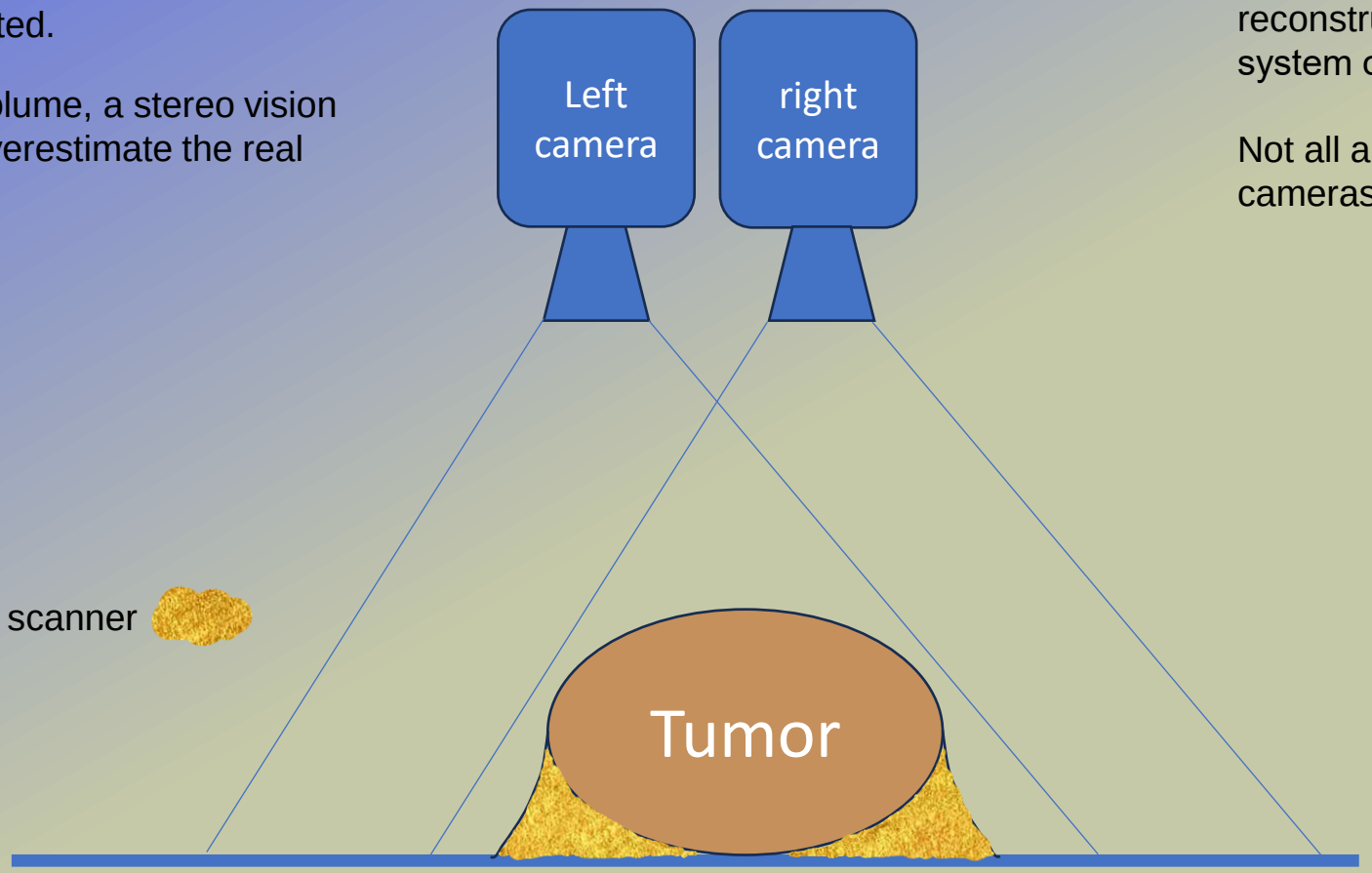
The tumor volume measurement series, Tm900, uses an advanced stereo vision and 3D reconstruction algorithm. For spherical objects and their volume calculation, one must take into consideration the “mushroom” effect, as explained in this image.

Areas not visible for both cameras will not be reconstructed.

For a spherical volume, a stereo vision 3D method will overestimate the real volume.

$V_{true} < V_{measured}$

Volume added by scanner



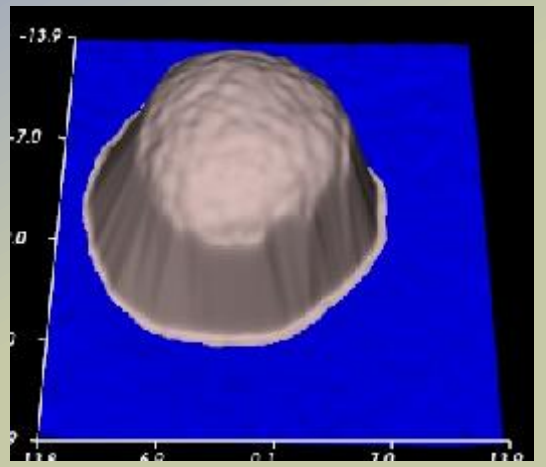
The reconstructed surface will have a reconstructed artefact, as the camera system can not see “under” the tumor.

Not all areas are visible for both cameras

Plasticine tumor simulations

“Mushroom” effect in 3D scanner measurements on molded spheres

This image of a sphere shows how it is reconstructed by the scanner

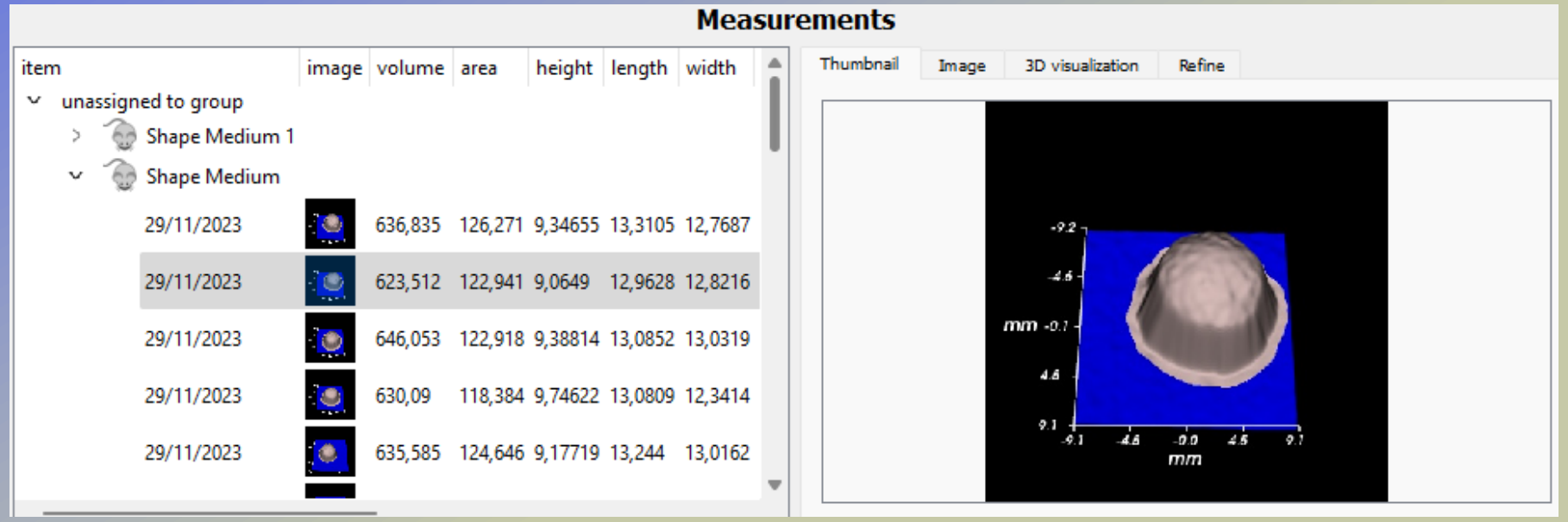


The volume generated by the scanner will be an over estimation of the real volume calculated. $4\ \pi\ r^3 / 3 = V_{real} < V_{TM900\ scanner}$

Plasticine tumor simulations

TM900v2 and caliper measurement, diameter sphere:

Three spheres, of sizes small, medium and big, were molded by hand. The diameter was measured by a vernier caller. A TM900 measurement will result in a volume, area, height, length and with of the region of interest, ROI, the white area in the right 3D reconstruction. Like in image:



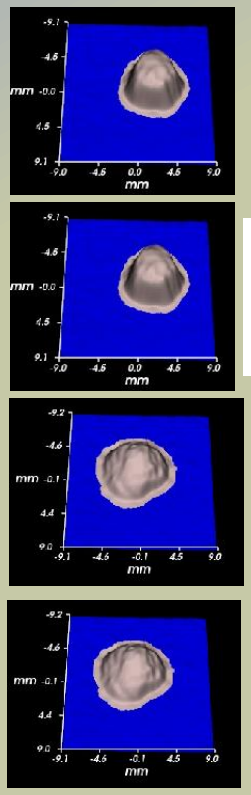
The height of the TM900v2 measured ROI should be close or the same as the diameter of the boll measured by caliper. Due to the mushroom effect, the width and length of the ROI will be oversized.

Due to the molding by hand the sphere will not be mathematically perfect. All measurements are good approximations, estimation, of real sizes and volumes.

Plasticine tumor simulations

In this experiment, 5 different values for the volumes of the different plasticine amounts were measured or calculated and are mapped in the next three slides:

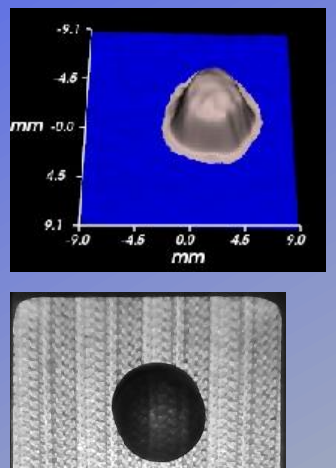
Sphere TM9002v		gives the volume output by the TM900v2 of the ROI, so including the reconstruction artefact
Spere Fomula Calculation		Is the volume calculated by the tumor volume formula v= 0,5*w*w*l, using width and length from the TM900v2 ROI, so a virtual caliper measurement
random shape TM900v2		Is the volume from the ROI of the molded tumor. As the amount of puddy is the same, these should correspond to the real sphere volume.
random shape Formula Calc.		Is the volume generated by the TM900v2 of the randomly shaped tumor like volume, , using width and length from the TM900v2 ROI, so a virtual caliper measurement. This volume should be close or similar to the real volume.
Estimation		Is the refference volume, close to the real volume, based on diameter measurement by caliper of the sphere and the formula of a boll, 4 $\pi r^3 / 3$.

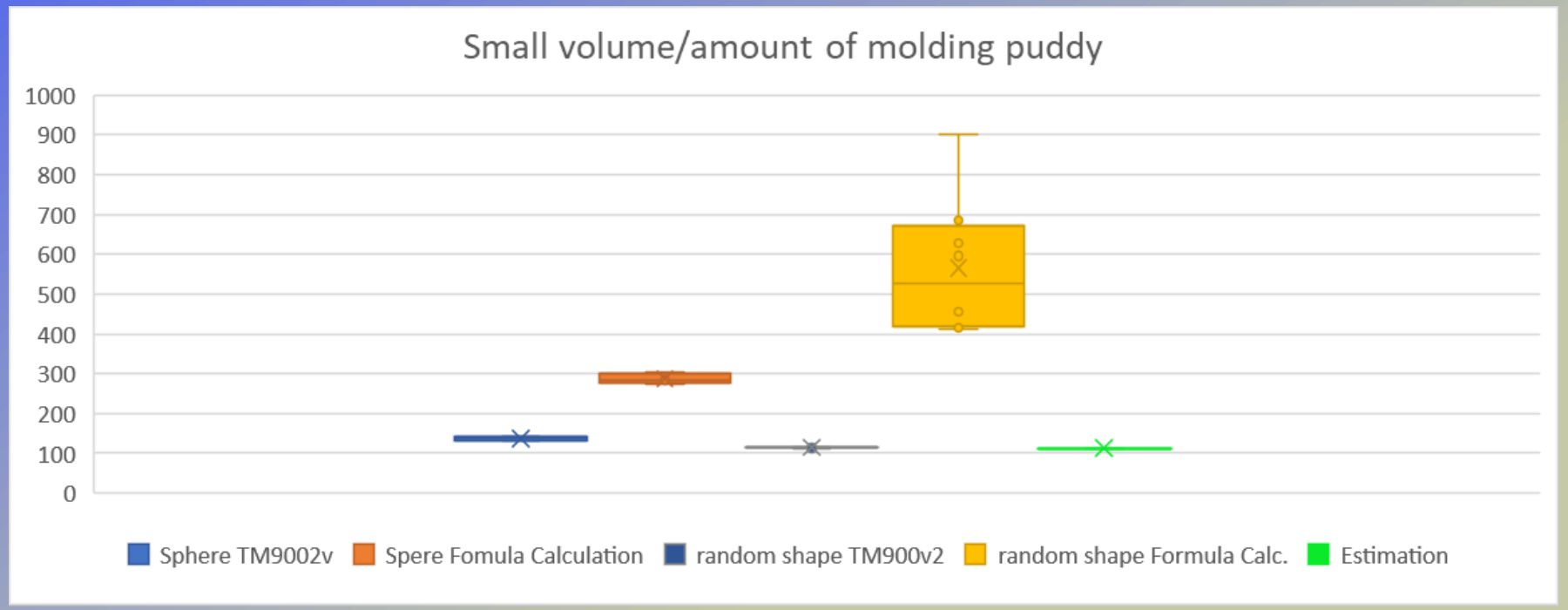


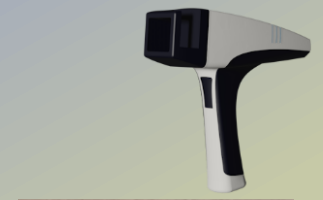
$$V = \frac{l\,w^2}{2}$$

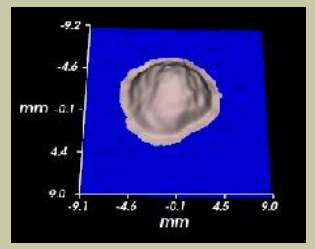
$$V = \frac{l\,w^2}{2}$$

Plasticine tumor simulations



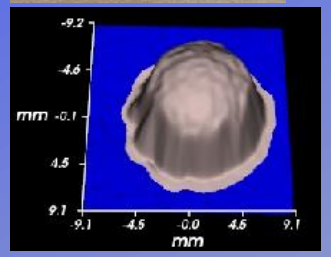


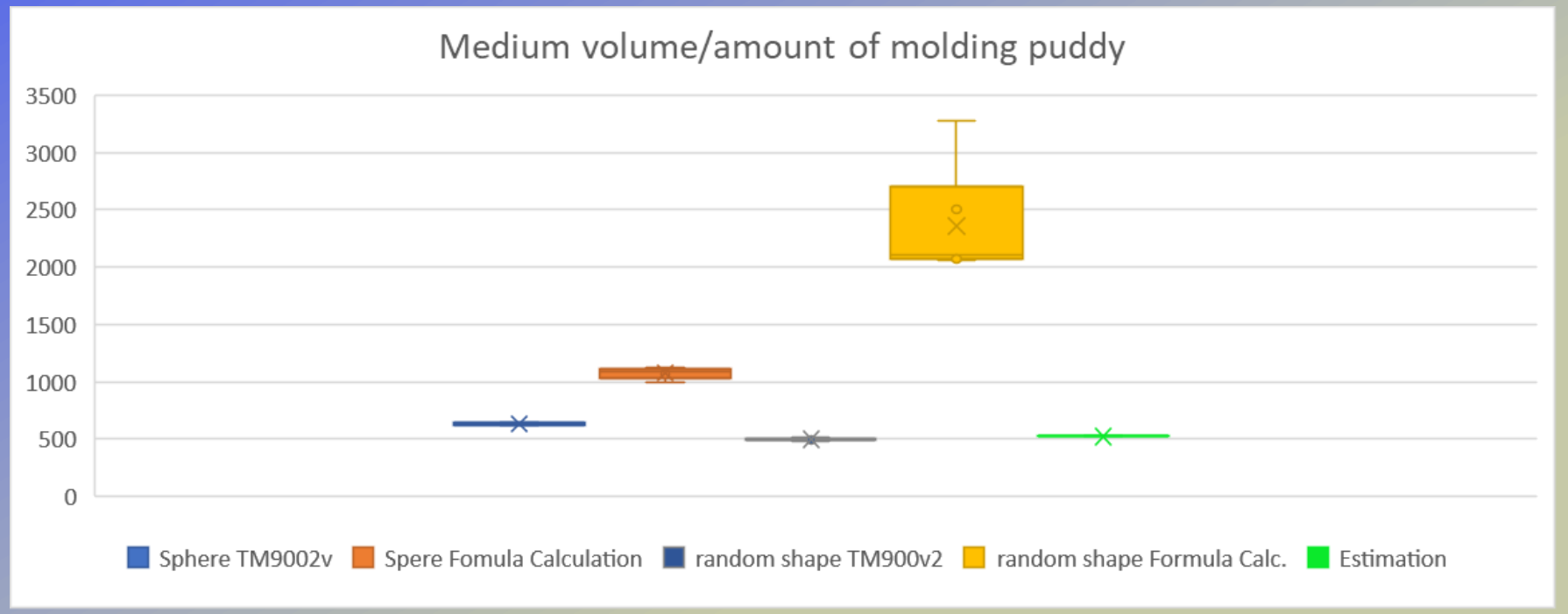


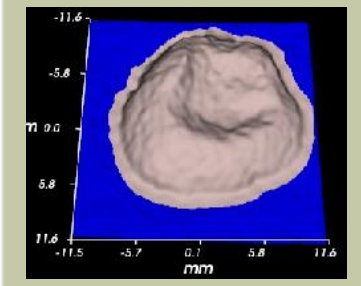


Sphere TM9002v	137	mm^3	
Spere Fomula Calculation	287	mm^3	
random shape TM900v2	114	mm^3	
random shape Formula Calc.	566	mm^3	
Estimation	113	mm^3	base on diameter measurement sphere

Plasticine tumor simulations

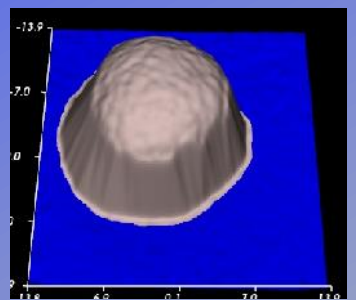


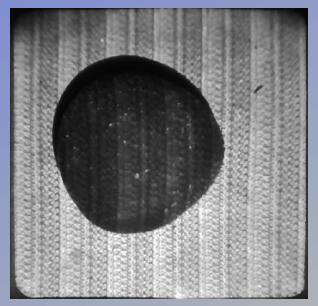


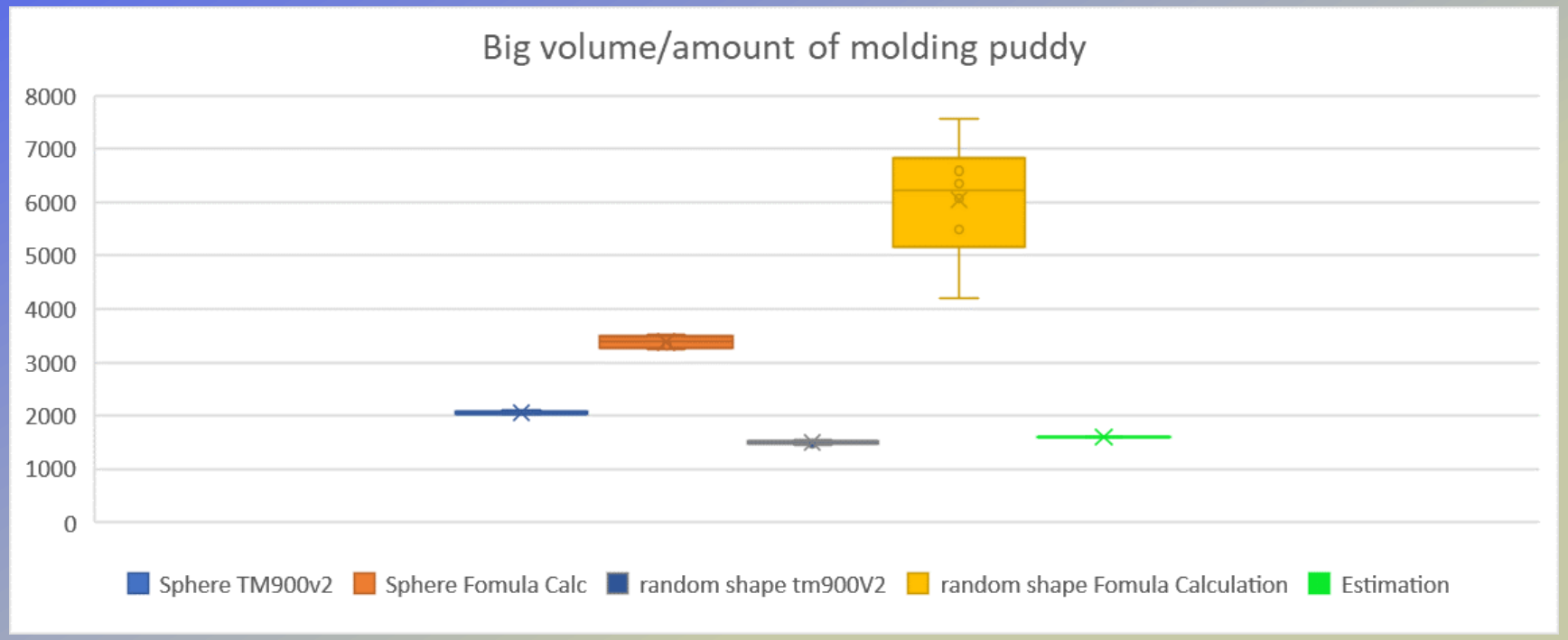


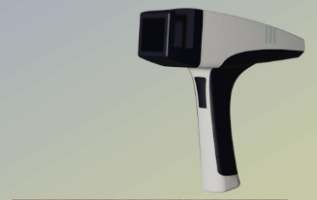
Sphere TM9002v	634	mm^3	
Spere Fomula Calculation	1076	mm^3	
random shape TM900v2	499	mm^3	
random shape Formula Calc.	2356	mm^3	
Estimation	523	mm^3	base on diameter measurement sphere

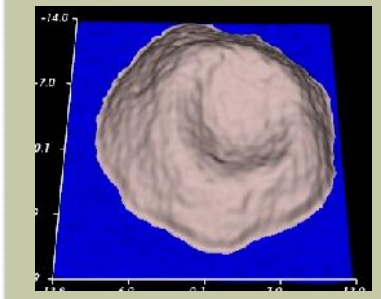
Plasticine tumor simulations











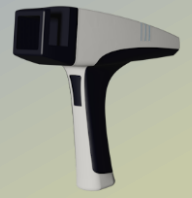
Sphere TM9002v	2050	mm^3	
Spere Fomula Calculation	3387	mm^3	
random shape TM900v2	1502	mm^3	
random shape Formula Calc.	6048	mm^3	
Estimation	1595	mm^3	base on diameter measurement sphere

Plasticine tumor simulations

The real volume of the plasticine amount, labeled as “estimation”, is calculated and used as reference for the real volume/amount.

These results show that the volumes, Sphere formula calculation and random shape formula calculation, calculated by the tumor volume formula with the width and length are significant overestimations.

The TM900v2 measurements closely match the real volume. As expected, the TM900 measurement of the spere, Sphere TM900v2, is higher than the real volume estimation. The randomly shaped tumor expression like shapes, random shape TM900v2, are closely matching the real volume.



Subcutaneous and extracted tumor

Description of the experiment:

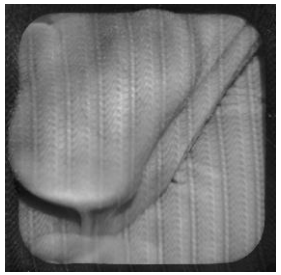
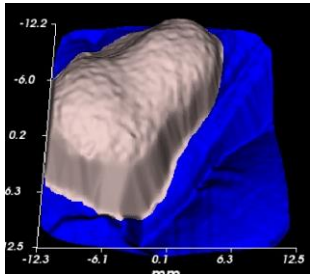
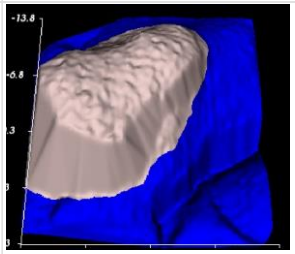
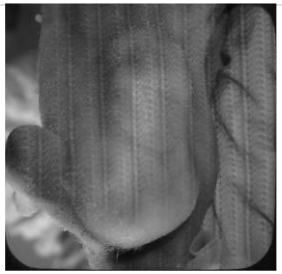
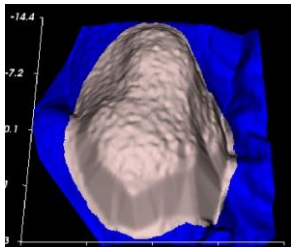
For three animals with tumors at different stages of growth, of different sizes, small, medium and big, TM900 measurements were done of the subcutaneous tumor in the animal. The measurement was done three times, by three different operators. This induced the operator and animal manipulation variability in the measurement.

After the TM900 measurement, the animals were sacrificed, and the tumors extracted. The then separated tumors were put on a paper tissue and measured by the TM900. These measurements were also done multiple times, with different orientation of the measurement instrument over the tumor.

With the width and length from the TM900 measurement, the volume was calculated using two of the most commonly used tumor volume formulas. These results are simulation of- and used as caliper measurements for comparison of the data.

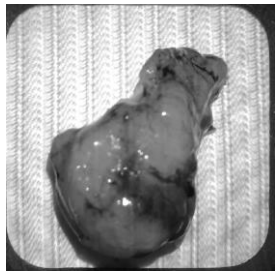
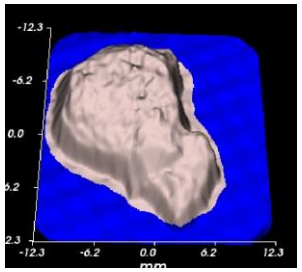
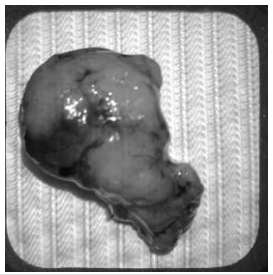
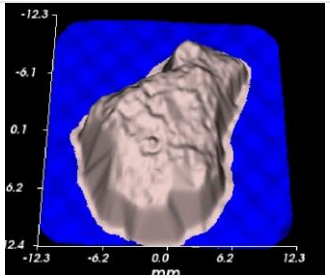
Following slides present the data and comparison.

Subcutaneous and extracted tumor

A big Tumor in an animal		TM900 Results				$V=\frac{l\,w^2}{2}$		$V=\frac{\pi\,l\,w^2}{6}$	
		height	width	length	TM900	Avg TM900	Calc	Avg Calc	Calc	Avg Calc
		9,2977	15,91	23,686	1437,55		2996,92		3136,77	
		9,0915	19,96	21,645	1425,05	1601,76	4311,79	4017,29	4513,00	######
		10,109	19,3	25,473	1942,67		4743,17		4964,52	

During the first two measurements, due to its size, the tumor was not positioned correctly, it partially was outside the imaged area.

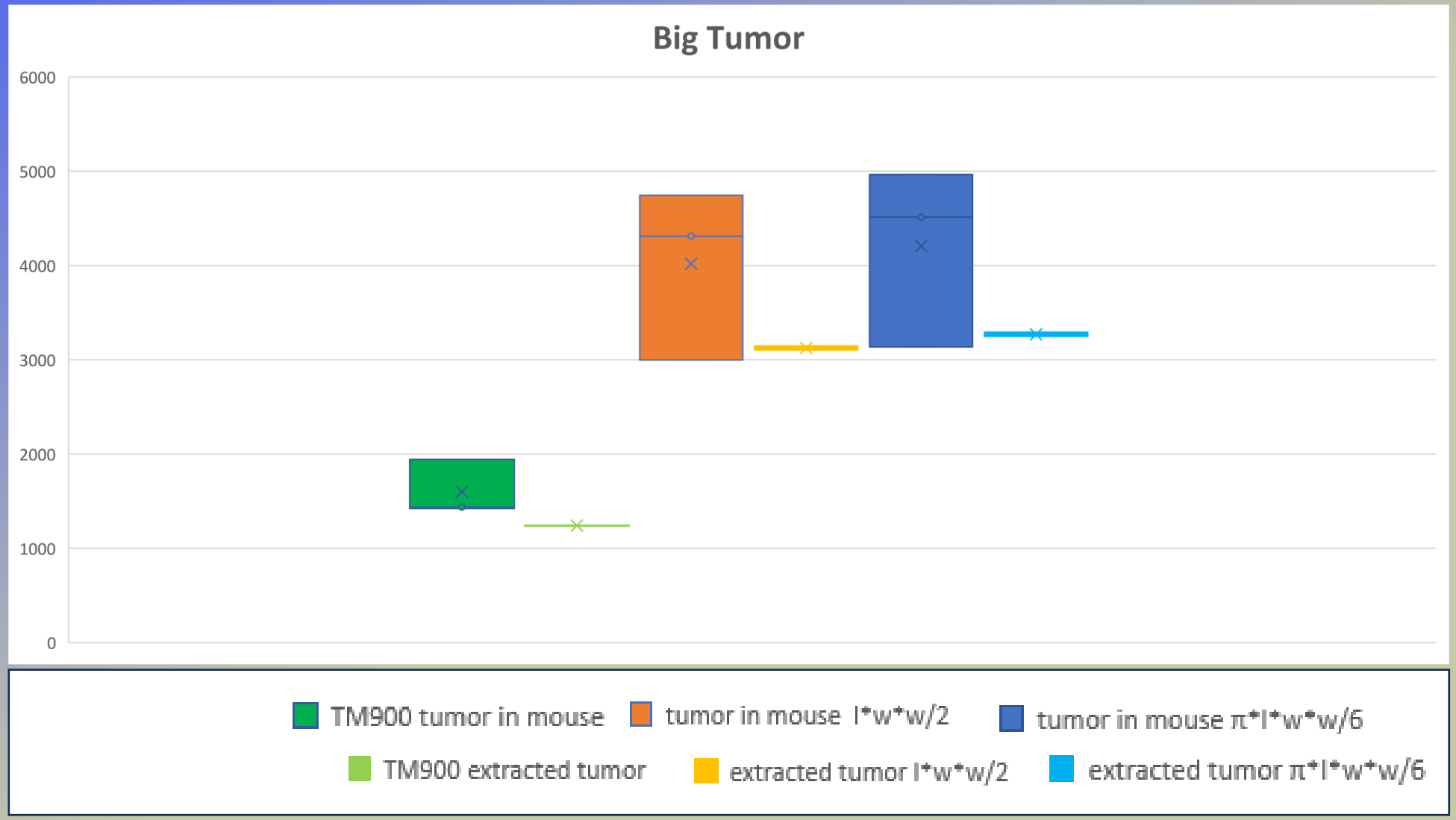
Subcutaneous and extracted tumor

The same big tumor, extracted		TM900 Results				$V = \frac{l w^2}{2}$		$V = \frac{\pi l w^2}{6}$	
		height	width	length	volume TM900	Avg TM900	Calc	Avg Calc	Calc	Avg Calc
		9,1207	17,25	21,142	1237,47	1240,85	3144,96	3124,08	3291,73	3269,87
		8,903	16,85	21,858	1244,23		3103,20		3248,02	

The “mushroom” effect is visible, the volume of the spherical shaped tumor oversized.

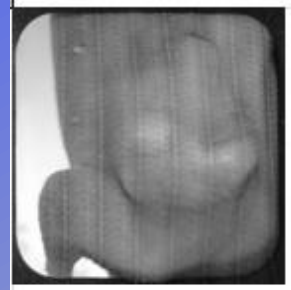
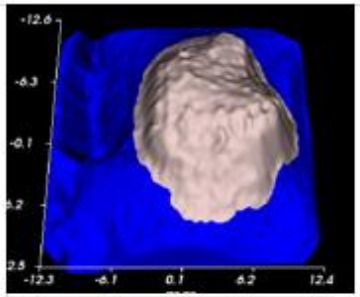
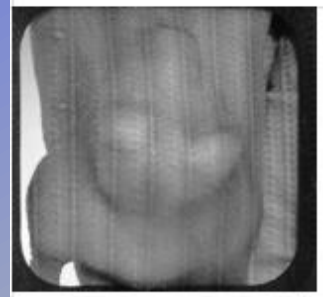
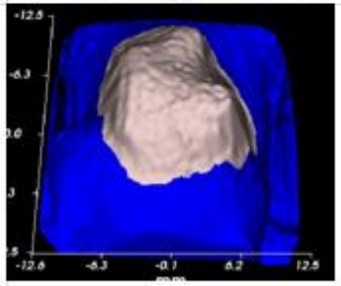
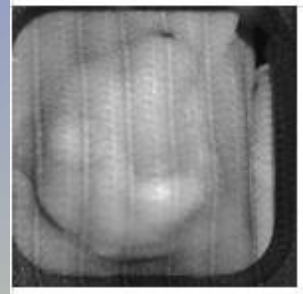
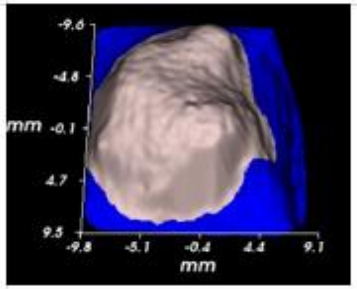
Conclusion: The real volume for this tumor V_{tumor} <1240mm^3.

Subcutaneous and extracted tumor



Subcutaneous and extracted tumor

Medium Tumor in animal

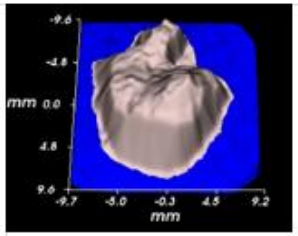
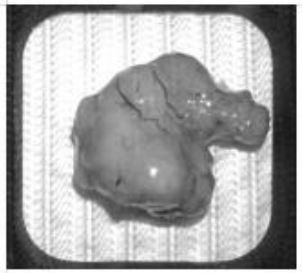
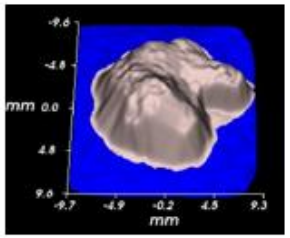
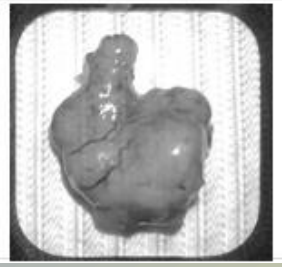
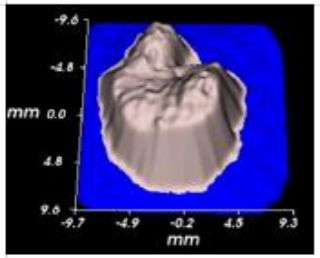
TM900 Results

$V = \frac{l w^2}{2}$

$V = \frac{\pi l w^2}{6}$

height	width	length	volume TM900	Avg TM900	FormulaCalc	Avg Calc	FormulaCalc	Avg Calc
7,61173	15,1635	17,9656	774,311		2065,43		2161,82	
7,21261	14,6422	18,1014	775,262	775,03	1940,42	1996,77	2030,97	2089,95
7,42755	15,4029	16,7289	775,507		1984,46		2077,07	

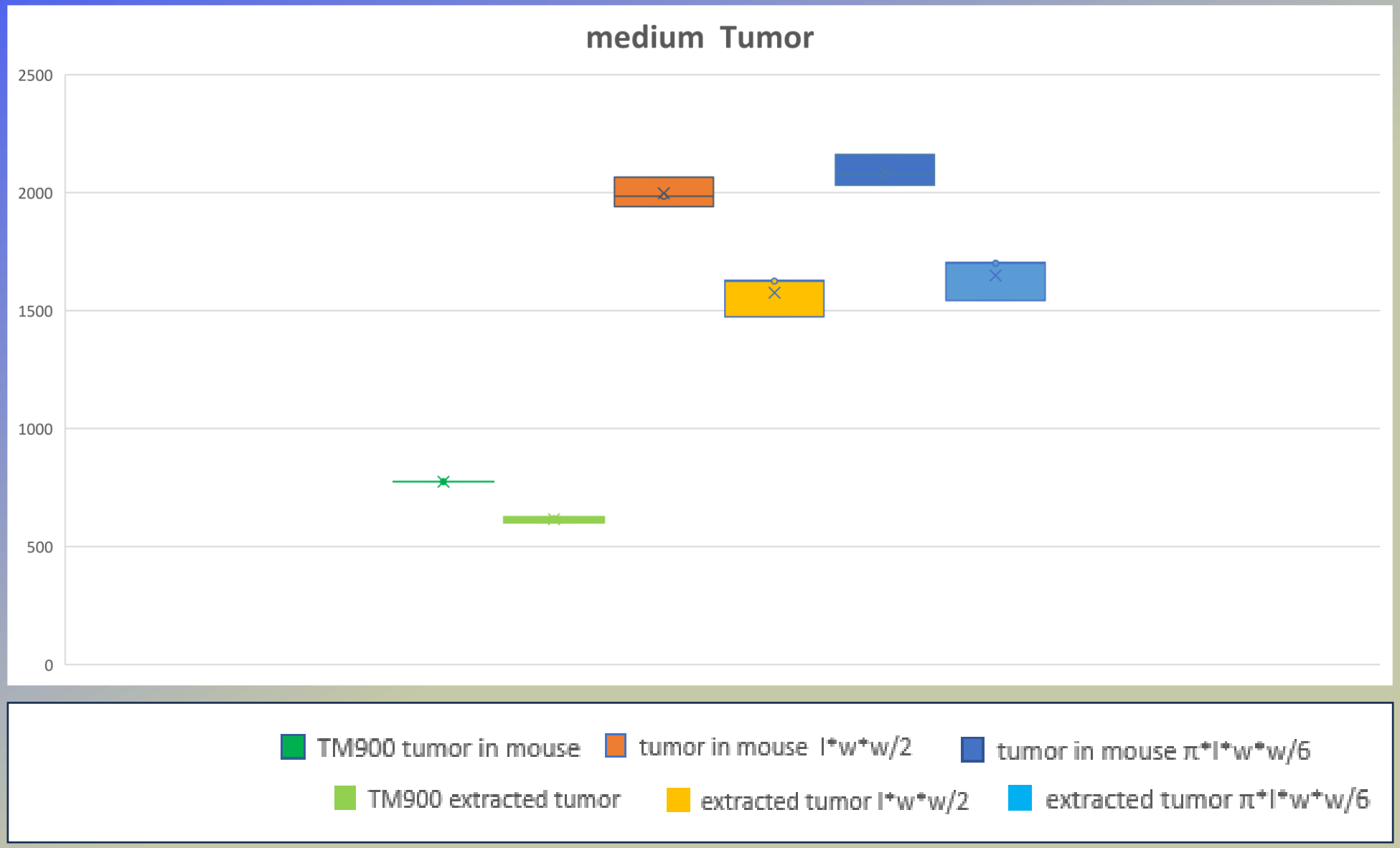
Subcutaneous and extracted tumor

Same medium tumor, extracted		TM900 Results				$V=\frac{l\,w^2}{2}$		$V=\frac{\pi\,l\,w^2}{6}$	
		height	width	length	volume TM900	Avg TM900	FormulaCalc	Avg Calc	FormulaCalc	Avg Calc
		8,54451	14,4671	15,5262	618,802	615,47	1624,79	1575,68	1700,62	1649,21
		8,16798	14,6638	15,1486	627,045		1628,68		1704,68	
		8,55128	14,0493	14,931	600,55		1473,56		1542,33	

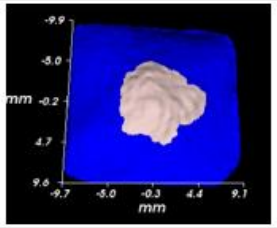
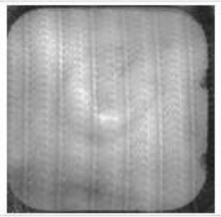
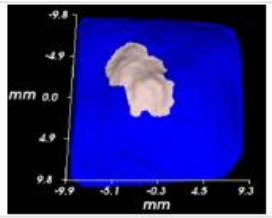
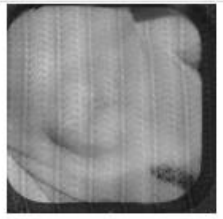
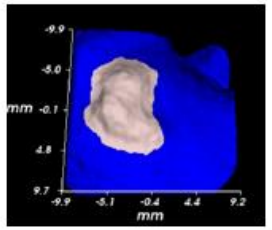
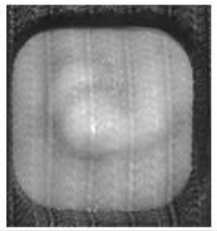
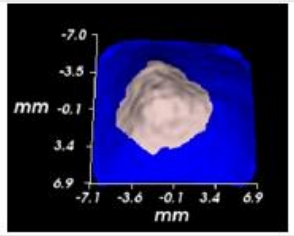
The “mushroom” effect is visible, the volume of the spherical shaped tumor oversized.

Conclusion; The real volume for this tumor $V_{tumor} < 615mm^3$.

Subcutaneous and extracted tumor

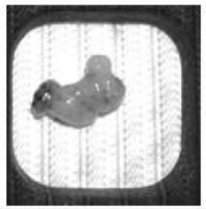
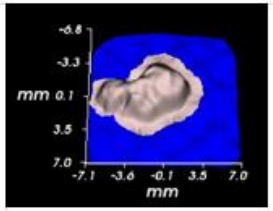
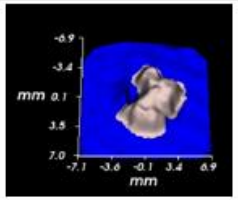
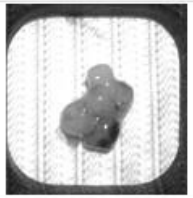
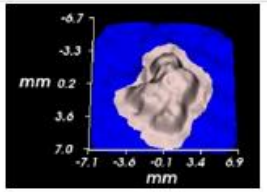
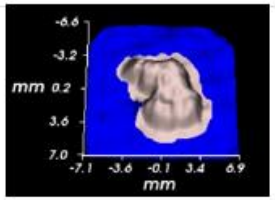


Subcutaneous and extracted tumor

Small tumor in animal		TM900 Results					$V=\frac{l\,w^2}{2}$		$V=\frac{\pi\,l\,w^2}{6}$	
		height	width	length	volume TM900	Avg TM900	FormulaCalc	Avg Calc	FormulaCalc	Avg Calc
		1,62666	8,67884	9,62477	40,0381		362,48		379,40	
		1,1632	6,07688	9,522	19,6459		175,82		184,02	
		2,62172	8,34787	10,5654	71,5129	42,82	368,14	268,92	385,31	281,47
		2,1336	6,70847	7,52138	40,0879		169,24		177,14	

Variability in measurement is due to different expression of the tumor from under the skin. Animal manipulation, skin stretching can cause this.

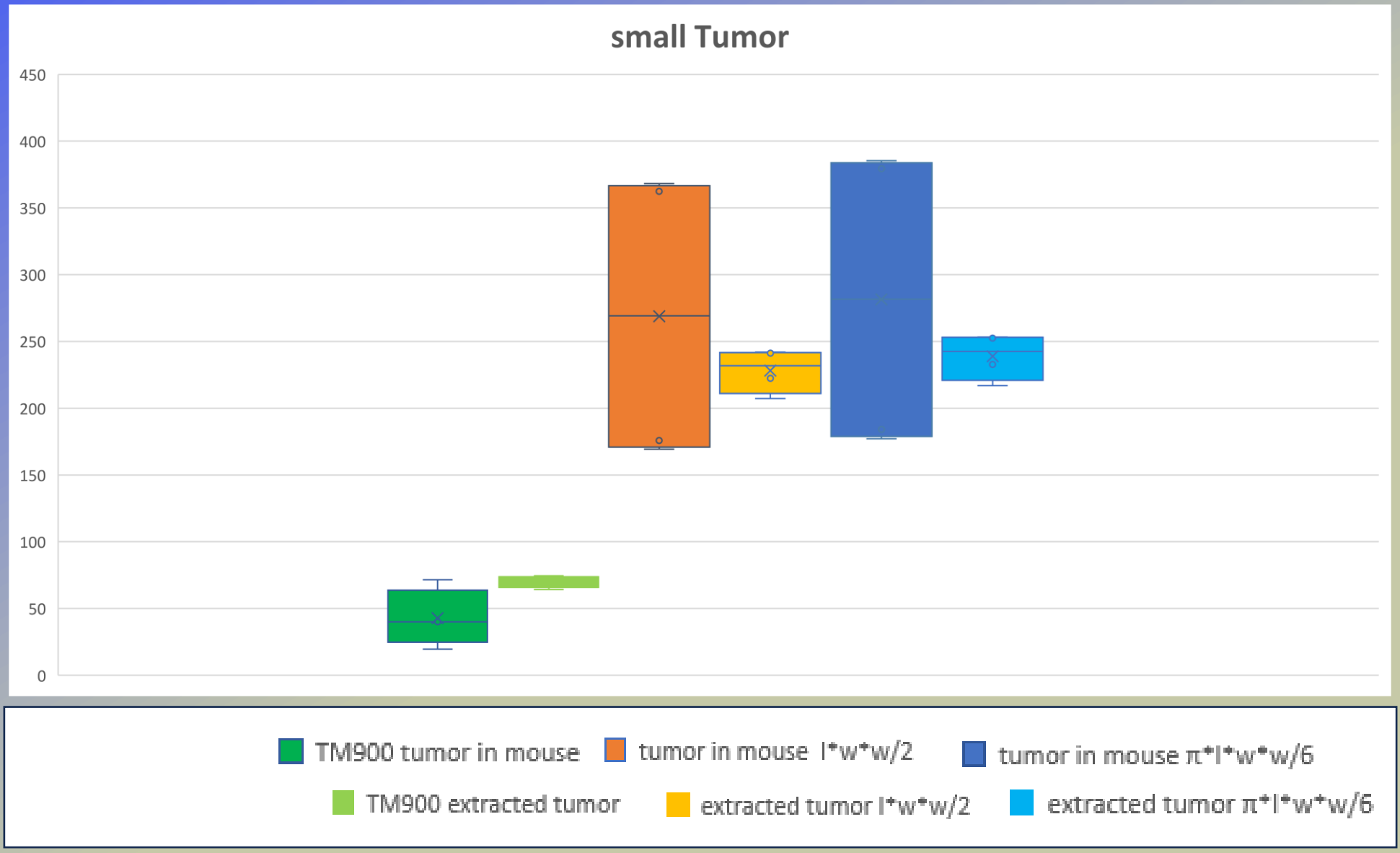
Subcutaneous and extracted tumor

The same small tumor, extracted		TM900 Results				$V=\frac{l w^2}{2}$		$V=\frac{\pi l w^2}{6}$	
		height	width	length	volume TM900	Avg TM900	FormulaCalc	Avg Calc	FormulaCalc	Avg Calc
		3,41052	6,69561	9,92116	70,2337		222,39		232,77	
		3,56239	6,99603	8,46618	64,2247	70,10	207,19	228,17	216,85	238,81
		3,3947	7,44271	8,73489	71,4146		241,93		253,22	
		3,34469	7,11269	9,53395	74,519		241,16		252,42	

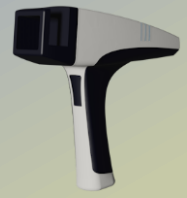
The “mushroom” effect is visible, the volume of the spherical shaped tumor oversized.

Conclusion; The real volume for this tumor is <70mm^3.

Subcutaneous and extracted tumor



During a study, formula calculations vs TM900v2

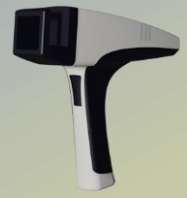


Description of the experiment:

In this test, 4 animals were monitored with the TM900v2. During a three weeks study. The volume data from the scanner were plotted against the volume that is calculated using the tumor volume formula. For this the width and length data obtained by the TM900v2 were used in the calculations. So not physical caliper measurements were done.

Following slides provide the actual data and graphical comparisons.

During a study, formula calculations vs TM900v2



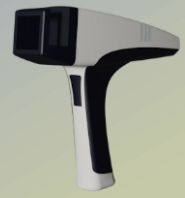
animal tag	Day	volume TM900v2	height	width	length	Fomula v=0,5*w*w*l
001	1	11,8955	1,23797	5,12998	5,95842	78,40296032
001	3	37,9025	2,00233	6,95247	7,05323	170,4654218
001	6	105,625	2,76063	8,78698	10,1839	393,1546407
001	10	117,767	2,61857	10,4124	10,9206	591,9952082
001	14	1209,13	8,63797	16,6013	17,6014	2425,500745
001	17	2254,42	10,1195	21,9406	23,8065	5730,104665
001	19	2611,46	10,2099	22,926	24,9152	6547,732947

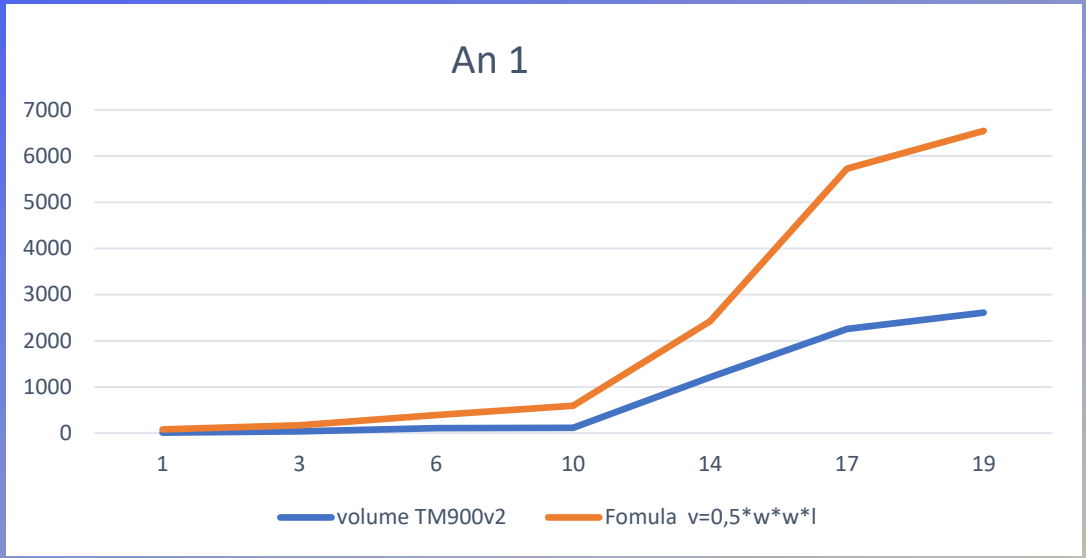
animal tag	Day	volume TM900v2	height	width	length	Fomula v=0,5*w*w*l
002	1	21,4937	0,925171	6,54943	9,37072	200,9786733
002	3	21,2834	1,34826	6,92326	7,82946	187,6389946
002	6	37,625	2,13569	6,95124	8,07839	195,1728423
002	10	139,502	3,27104	9,24843	11,8628	507,3331496
002	14	598,004	6,81092	13,2556	16,6128	1459,52528
002	17	665,07	5,76822	13,8192	18,0696	1725,378364
002	19	1103,49	7,27666	15,3424	21,4667	2526,515075

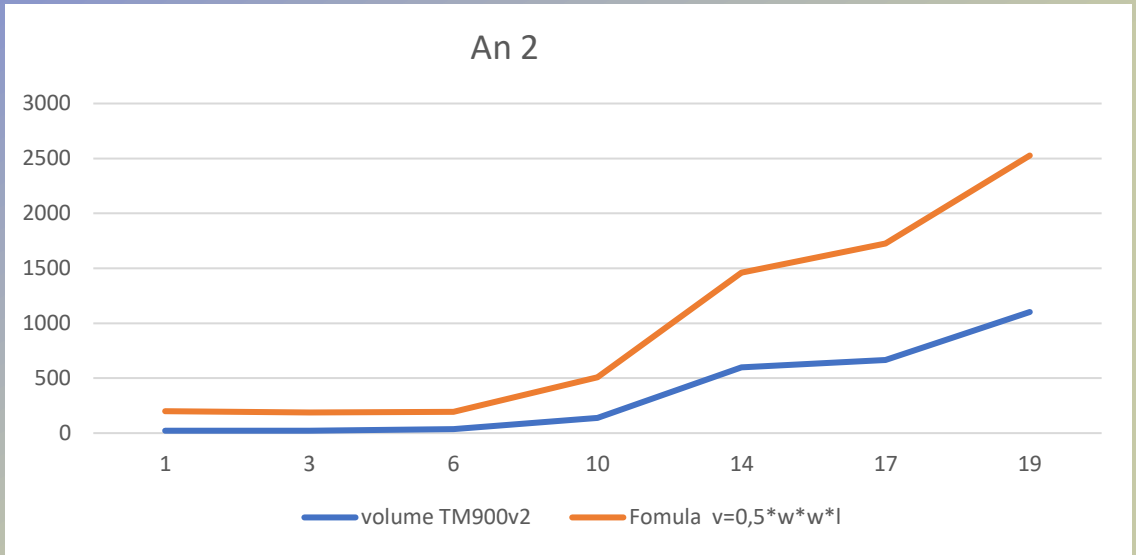
animal tag	Day	volume TM900v2	height	width	length	Fomula v=0,5*w*w*l
003	1	30,2114	1,56264	8,1312	8,52097	281,6879877
003	3	79,5195	2,64894	8,70998	10,015	379,8877361
003	6	171,321	3,61672	9,392	12,3853	546,2515758
003	10	510,803	5,73113	12,6428	16,9417	1353,983983
003	14	1714,68	9,32497	19,5003	19,7759	3760,008677
003	17	3440,53	12,9866	22,9505	26,1813	6895,178515
003	19	5088,17	13,5092	28,4013	28,8911	11652,26949

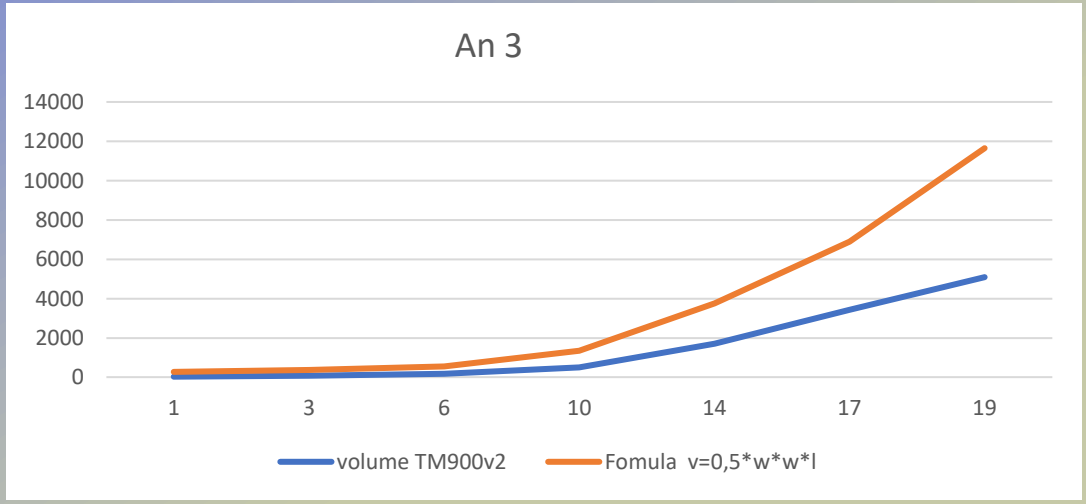
animal tag	Day	volume TM900v2	height	width	length	Fomula v=0,5*w*w*l
004	1	20,7961	1,22257	5,7467	8,92819	147,4247771
004	3	66,1518	2,62039	7,62072	9,76551	283,5678194
004	6	192,396	4,18853	10,076	11,5874	588,2098884
004	10	245,611	3,99969	10,9008	14,4011	855,6229277
004	14	352,197	5,3635	15,2012	16,4013	1894,977348
004	17	2598,89	10,7067	22,8917	23,7931	6234,148251
004	19	4816,91	15,8398	27,1438	27,5851	10162,15607

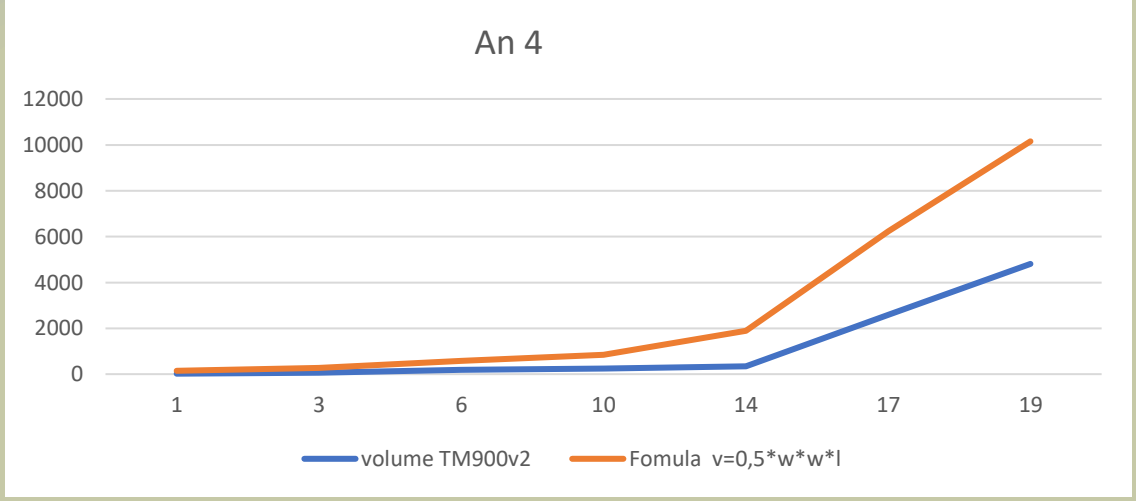
During a study, formula calculations vs TM900v2



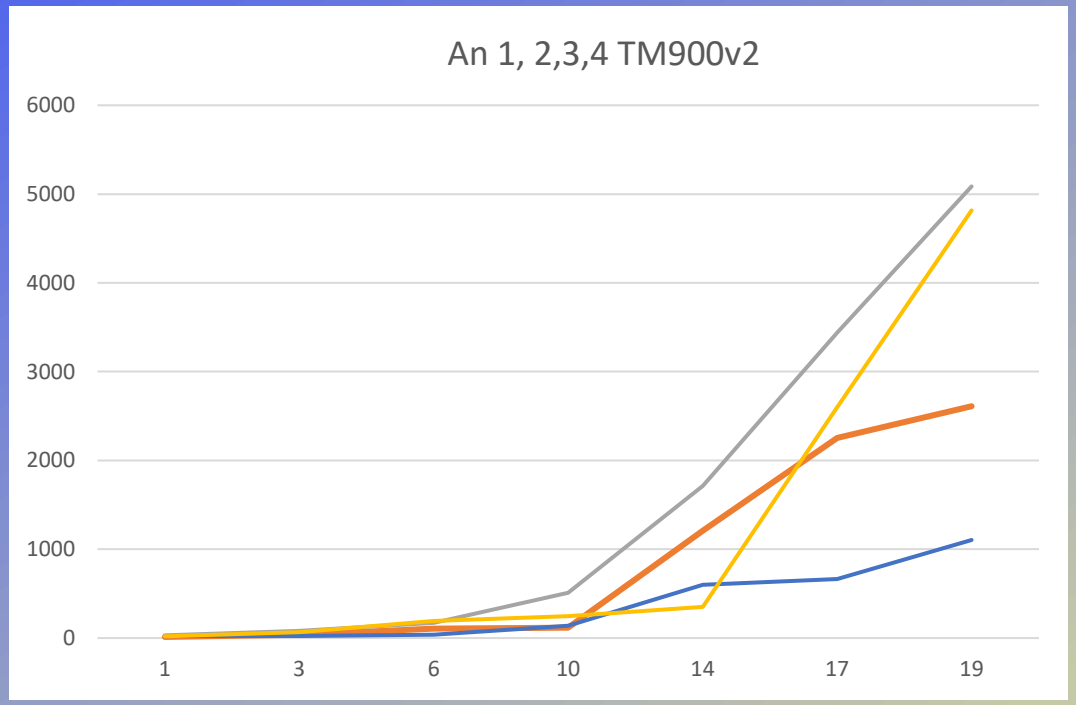


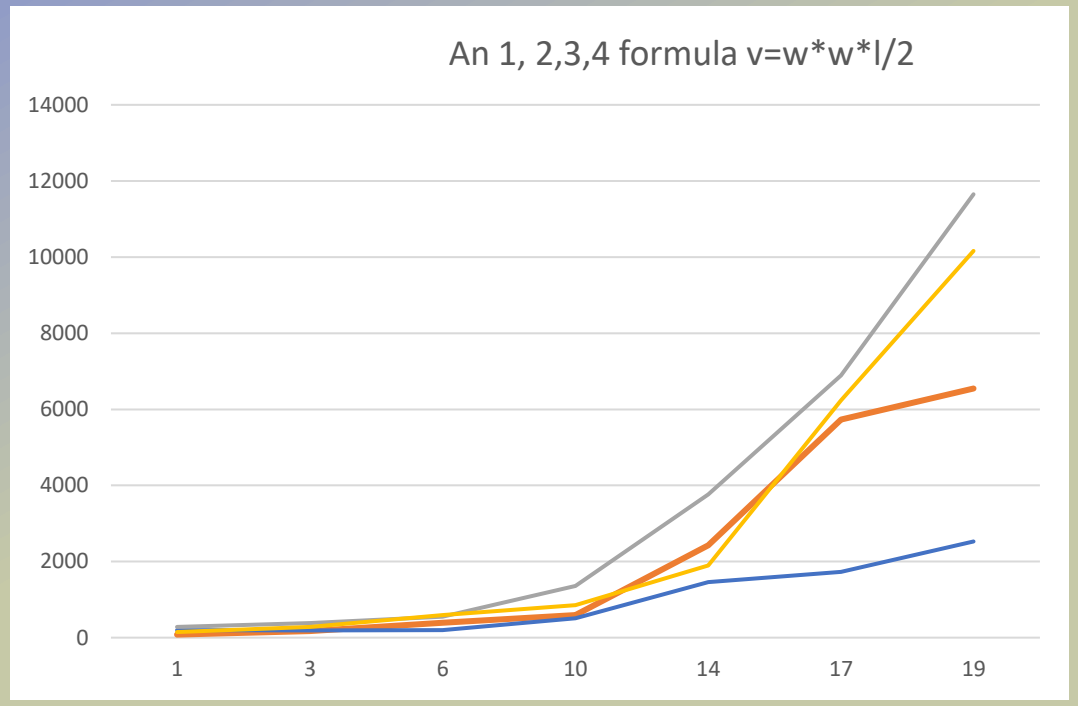




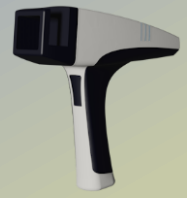


During a study, formula calculations vs TM900v2





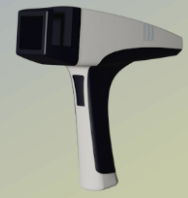
The graphs show that both methods generally do represent the same evolution in tumor volume changes. The lack in of height information in caliper measurements can affect the individual tumor data, the overall trend is similar.



Conclusions:

- Caliper measurements and tumor volume formulas highly overestimate the volume. TheTM900v2 volume measurements are significantly more accurate.
- TM900v2 measurements have a better match with real tumor volumes. The volume are a realistic upper limit on the real tumor volume: $V_{real} < V_{TM900v2\ scanner}$
- The standard deviation during a study for TM900v2 measurements is significantly less than with caliper measurements:
  - Caliper measurements lack tumor height changes, only width and length variations will affect the volumes calculated.
  - During caliper measurements, differences in measured width and length will significantly influence the volume calculated.

The effect of inaccuracies, in caliper measurement-based tumor volume monitoring, due to height and with variability and the lack of height information is shown on: https://tumorvolume.com/peira-tm900-caliper-measuremet/



For more information:

https://tumorvolume.com/contact/

https://budetec.be/contact/