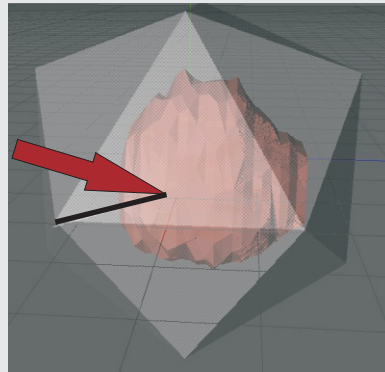


# Anwendung der Formanalyse zur Klassifikation von Nierentumoren (3D) im Kindesalter



M.A./Dipl. Math. /Cand. Soz. päd.)

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# Overview

1) Survey

2) Shape

3) Mean Shape

4) Tests

5) Differences  
between tumours  
shown in an optical way

6) Classification

- Conclusion
- Forecast

# Renal tumours appearing in early childhood

- Wilms- tumours growing in the near of the kidney  
*Genetic cause*  
*The majority of renal tumours in the childhood is diagnosed as “Wilms” (80%)*  
*There are four types of tissue (a, b, c, d) and three stages of development (I, II, III)*

- Renal cell carcinoma  
*growing also in the near of the kidney*  
*Are very rare in the childhood*  
*Many times in adulthood*

- Clear cell carcinoma  
*Growing in the near of bones .*  
*Are very rare*

- Neuroblastoma  
*Growing in the near of nerve tissue*  
*Also very rare*

- etc.

**Every kind of tumour needs its therapy. For diagnose there are a lot of magnetic resonance images.**

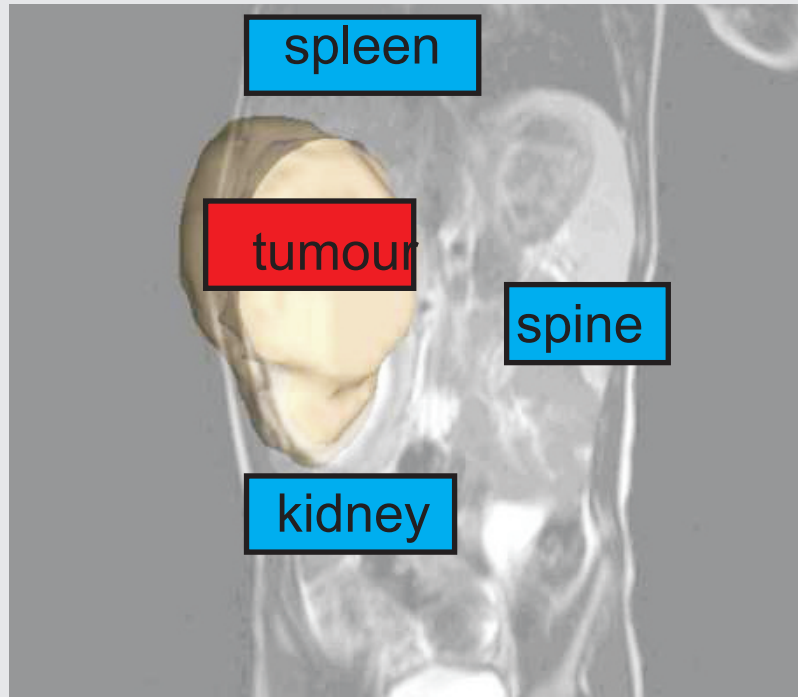
# Dicom Data



slides of data

**Getting transversal and frontal images of the tumour**  
**Problem: Not for each patient we have both views**  
**Images created by Magnetic resonance tomography**

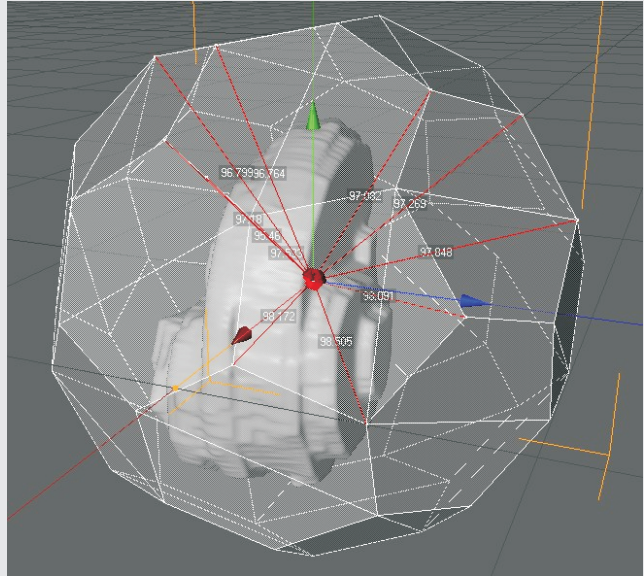
# Three-dimensional object



1. Construction by using the data (density, depth etc.)

# Explorative\* survey of landmarks

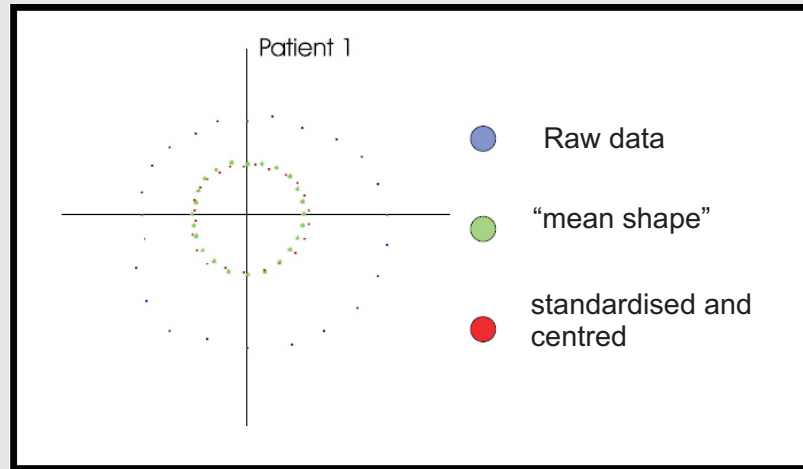
\*there are no medical relevant points used as landmarks



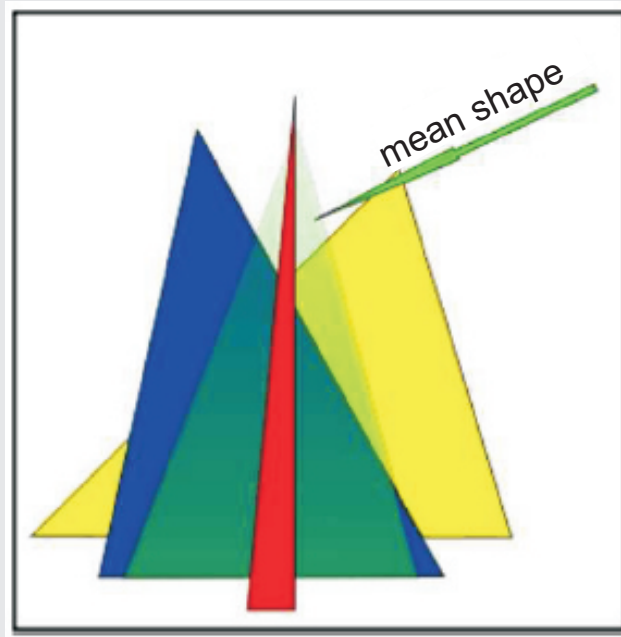
1. Determining of three dimensional mass point
2. Taking two dimensional image therein the mass point

# Data process

1. Standardisation (using Euclidean norm)
2. Centring on two-dimensional centre



# Determining of „mean shape“

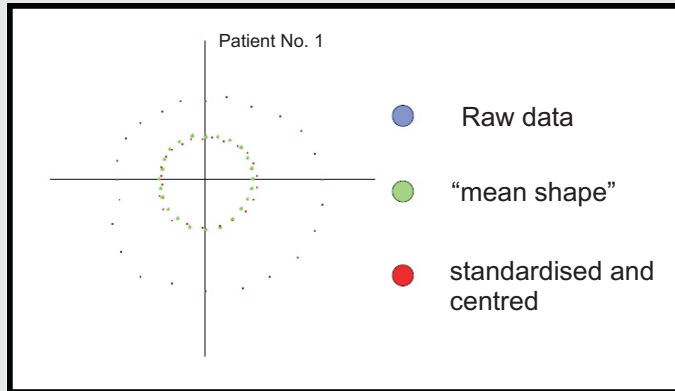


Determining the expected “mean shape” of a group of objects.

That mean's: smallest distance in the average to all shapes in the group



# Determining of “mean shape”



Using the following algorithm

$$i = 1, \dots, n$$
$$\tilde{m} \mapsto w_i(\tilde{m}) = \begin{cases} \frac{\langle \tilde{m}, o_i \rangle}{|\langle \tilde{m}, o_i \rangle|} & \text{if } \langle \tilde{m}, o_i \rangle \neq 0 \\ 1 & \text{if } \langle \tilde{m}, o_i \rangle = 0 \end{cases}$$

$$\tilde{m} \mapsto T(\tilde{m}) = \frac{1}{n} \sum_{i=1}^n w_i(\tilde{m}) o_i$$

recursively there is a sequence

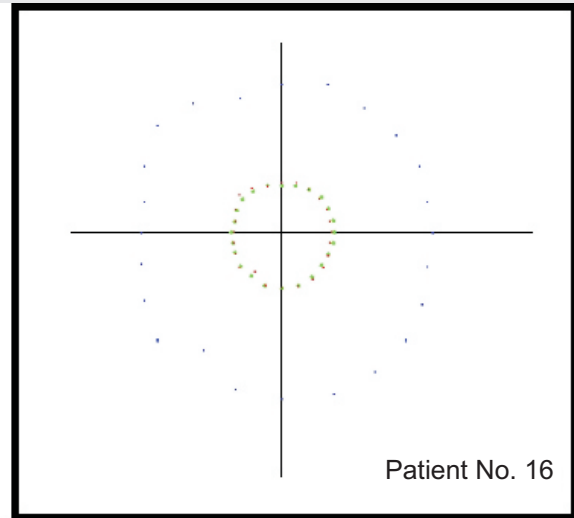
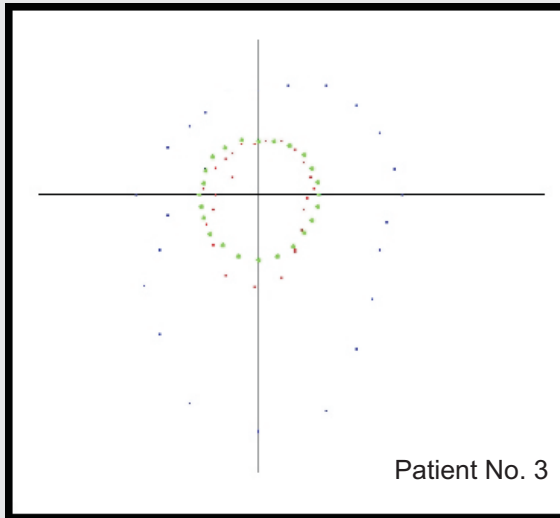
$$\tilde{m}_r = T(\tilde{m}_{r-1}), r = 1, 2, \dots \text{ iterations}$$

criterion to stop

$$\tilde{m} = T(\tilde{m})$$

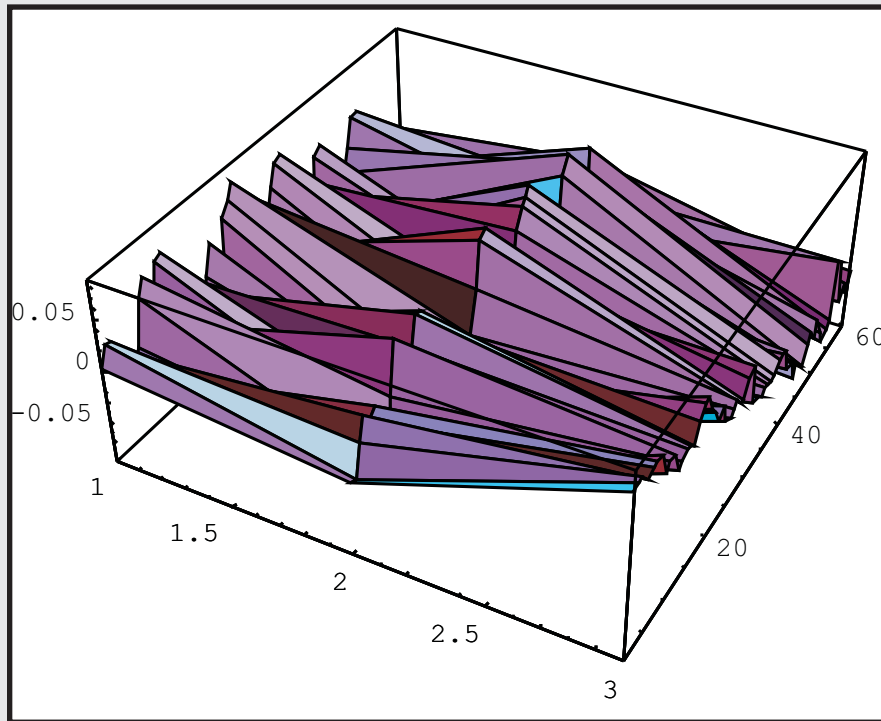
Algorithm for „mean shape“ (Ziezold 1994)

# Determining of „mean shape“

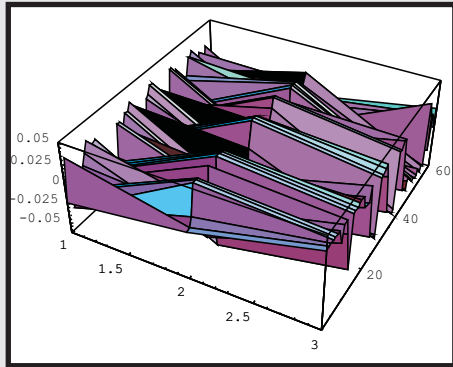


Statement: Patient No. 3 is very far from the “mean shape”.  
Patient No. 16 is very near to the “mean shape”.

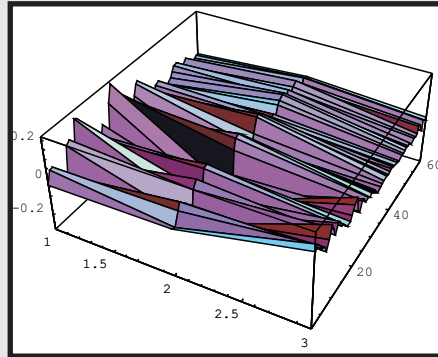
# Determining of “mean shape”



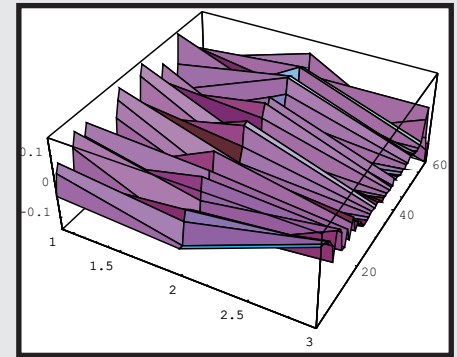
# Determining of „mean shape“



Patient No. 1  
 $d=0.359869$



Patient No. 9  
 $d=0,563754$



Patient No. 15  
 $d=0,535196$

# Distance from the “mean shape” (Wilms)

patient t		distance	
Nr.	Diagnose	$d_f$	$rangw$
Nr.1	n.b.	0.0849	3
Nr.2	IId	0.1009	6
Nr.3	IIf	0.2260	18
Nr.4	IIIf	0.0968	5
Nr.5	IIIf	0.1567	13
Nr.6	IIIf	0.1113	8
Nr.7	IId	0.1940	17
Nr.8	IId	0.1448	12
Nr.9	IId	0.1854	16
Nr.10	IIf	0.1290	11
Nr.11	IIIf	0.1834	15
Nr.12	IIIf	0.0772	2
Nr.13	IIf	0.0916	4
Nr.14	IIf	0.1058	7
Nr.15	IIf	0.1126	9
Nr.16	n.b.	0.0541	1
Nr.17	IIIf	0.1178	10
Nr.18	IIf	0.1754	14

# Distance from the “mean shape” (Wilms)

Patient Nr. 1	d=0.359859
Patient Nr. 2	d=0.559127
Patient Nr. 3	d=0.43159
Patient Nr. 4	d=0.519429
Patient Nr. 5	d=0.459117
Patient Nr 6	d= 0.467857
Patient Nr. 7	d= 0.491635
Patient Nr. 8	d=0.49588
Patient Nr. 9	d=0.563754
Patient Nr. 10	d= 0.492149
Patient Nr. 11	d=0.46524
Patient Nr 12	d=0.522007
Patient Nr. 13	d= 0.369287
Patient Nr. 14	d=0.435029,
Patient Nr 15	d=0.535196

# Description of the test (Ziezold, 1994)

The group of  $m$  objects is an independent realisation of the distribution  $P$  and the other group of  $k$  objects an independent realisation of the distribution  $Q$

Determining of  $p$ -value according to the test

$H_0: P=Q$

$H_1: P \neq Q$

**1. step:** Determining of “mean shape”

**2. step:** Determining of distances to the “mean shape” and the  $u_0$  according to the Mann-Whitney-U-Test

**3. step:** Determining all possible  $u$ -values separating the group ( $k+m$ ) in two groups with  $m$  and  $k$  objects

**4. step:** Determining the rank of  $u_0$  in the group of all  $u$ -values

**5. step:**  $p\text{-value} = r/N$

**6. step:** Determining the  $p$ -values in the other direction. Determining “mean shape” in the group of  $m$  objects

# Description of the test (Ziezold 1994)

**High**  $u_o$ -values means: A lot of cases - not used for the “mean shape”- has a smaller distance to the “mean shape” than the cases used for the “mean shape”

**Low**  $u_o$ -values means: Only a small number of cases - not used for the “mean shape”- has a smaller distance to the “mean shape” than the cases used for the “mean shape”

**Determining** of all possible permutations  
**possibilities**

brrr ●●●●  
rrbb .....  
rbbr .....  
brrb .....  
brbr .....  
rbrb ●●●●

$4! / (2! 2!) = 6$  possibilities

$|All| / (|subset_1|! |subset_2|!) = \text{Number of all possibilities}$



# Checking of differences between types of

Subsets		Differentiation					
Tumortyp 1	Tumortyp 2	$u_0$	$m_{=}$	$m_{<}$	$p - Intervall$	k	$\binom{15}{k}$
$\overline{Typ\ a}$	$\overline{Typ\ a}$	0	57	0	[0.002, 0.125]	3	455
$\overline{Typ\ a}$	$Typ\ a$	21	14	338	[0.745, 0.774]	12	455
$\overline{Typ\ b}$	$\overline{Typ\ b}$	2	22	64	[0.619, 0.819]	2	105
$\overline{Typ\ b}$	$Typ\ b$	9	5	37	[0.362, 0.409]	13	105
$\overline{Typ\ c}$	$\overline{Typ\ c}$	6	17	431	[0.086, 0.090]	6	5005
$\overline{Typ\ c}$	$Typ\ c$	14	155	780	[0.156, 0.187]	9	5005
$\overline{Typ\ d}$	$\overline{Typ\ d}$	17	52	970	[0.711, 0.749]	4	1365
$\overline{Typ\ d}$	$Typ\ d$	10	40	153	[0.113, 0.141]	11	1365

$m_{=}$  ...: Number of cases with the same u-value  
 $m_{<}$  ...: Number of cases with a lower u-value  
 The interval is a result of the smallest and the highest rank of  $u_0$ .

# Checking of differences between different tumours

Subsets		Differentiation						
Tumortyp 1	Tumortyp 2	$u_0$	$m_{=}$	$m_{<}$	$p - Intervall$	k	n	$\binom{n}{k}$
Wilms	N1	12	47	122	[0.0924, 0.1271]	3	21	1330
N1	Wilms	15	36	834	[0.6271, 0.6541]	18	21	1330
Wilms	K	5	4	13	[0.0737, 0.0895]	2	20	190
K	Wilms	0	103	0	[0.0053, 0.5421]	18	20	190
Wilms	N2	11	3	11	[0.6667, 0.7778]	18	19	18
K	N1	0	7	0	[0.1, 0.7]	2	5	10
N1	K	1	2	5	[0.6, 0.7]	3	5	10
K	N2	0	3	0	[0.3333, 1]	2	3	3
N1	N2	1	2	1	[0.5, 0.75]	3	4	4

$m_{=}$  ...: Number of cases with the same u-value  
 $m_{<}$  ...: Number of cases with a lower u-value  
 The interval is a result of the smallest and the highest rank of  $u_0$

# Checking of differences between different tumours

## Non-Wilms - Wilms

u=61 rank=939 random sample: n= 1000 p=0.939

## Wilms - Non-Wilms

u=49 rank=29  
random sample: n= 1000  
p=0.029

# Checking of differences between different tumours

## Neuroblastoma - Wilms

$u=2$  rank=78 random sample:  $n=1000$   $p=0.078$

## Wilms - Neuroblastoma

$u=25$  rank (up)=40 rank (down)=15

random sample:  $n=1000$

$p=0.04$   $p=0.015$

# Conclusions

Typ c and clear cell carcinoma have a tendency for differentiation

Neuroblastoma only in one direction

Renal cell carcinoma not differentiable

In 3 dimension: Neuroblastoma and Wilms in both directions

In 3 dimension Wilms have a mean shape for differentiating

# Independence (Influence) of Landmarks of Shape

Ziezold • Mathematische Schriften Kassel, Heft 03/2003

$H_0$  The  $k$ th landmark of  $X$  is independent (influenced by) of the other landmarks with respect to the distance

$H_1$  The  $k$ th landmark of  $X$  is not independent (influenced by) of the other landmarks with respect to the distance

Step 1.

$$A_p = A_p^1 = \frac{1}{n - n_p} \sum_{d(\mathbf{x}^{(i)'}, \mathbf{x}^{(j)'}) > c_p} \frac{|x_{ik} - x_{jk}|}{d(\mathbf{x}^{(i)'}, \mathbf{x}^{(j)'})}$$

Distance between Landmarks

Distance between Objects

$$A_p^s = \frac{1}{n - n_p} \sum_{d(\mathbf{x}^{(i)'}, \mathbf{x}^{(j)'}) > c_p} \frac{|x_{\tau_s(i),k} - x_{\tau_s(j),k}|}{d(\mathbf{x}^{(i)'}, \mathbf{x}^{(j)'})}$$

Random selected

Step 2.

$$R_p = \text{rank}(A_p^1, \{A_p^1, A_p^2, \dots, A_p^N\})$$







Step 3.

$$\pi_p = \frac{N - (R_p - 1)}{N} \leq \alpha \text{ i.e. } R_p \geq N(1 - \alpha) + 1$$

p - value

# Explanation of test

## Constellation

landmark numerator	object without landmark denominator
	
	
	

## Possibilities

landmark numerator	object without landmark denominator
	
	
	

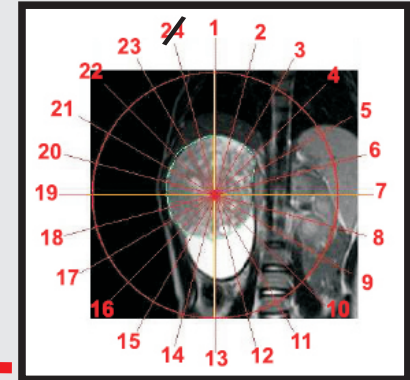
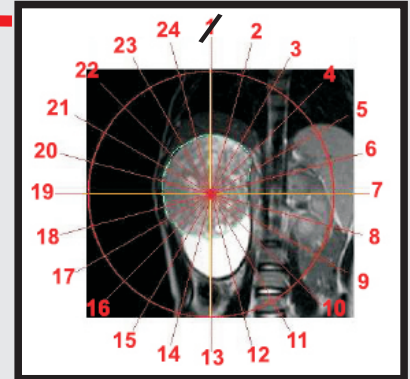
We want to test the real constellation to all possibilities

# Landmark Rank

Results  
for  
p-quantil = 65%

In the case  
of 2D

1	45/46
2	48/49
3	34/35
4	39
5	54/55
6	43
7	40
8	39
9	33
10	46/47
11	48
12	45/46
13	43
14	35/36/37
15	42
16	34
17	30
18	30
19	32
20	35
21	31/32/33
22	49
23	43
24	42





# Wilcoxon - Test

Also it is interesting to test the landmarks for differentiating nephroblastoma to neuroblastoma. For that test we use the Wilcoxon-Test. We assume that the average of difference to the mean shape for every landmark can be used for differentiating the tumors.

Wilms / Neuroblastome  
 $p \in [0,1887; 0,1917]$

In  
2D

Neuroblastome / Wilms  
 $p \in [0,7586; 0,763]$

No results for  $= 0,1$

Wilms Landm.  $\xrightarrow{d}$  Mean shape  
Landmark 1

Neuro Landm.  $\xrightarrow{d}$  Mean shape  
Landmark 1

$d_1 \dots d_{24}$

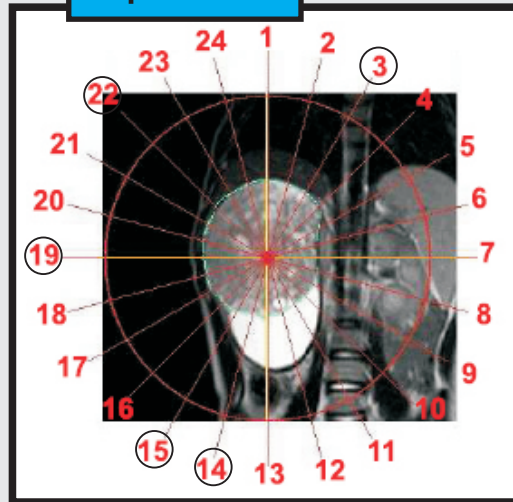
# Explorative take k=5 landmarks from 24

1. One sample for best configuration  
(small = u-value for differentiating neuro/wilms)
2. One sample for test

Relevant  
results for  
medicine

limit of  
body

spleen

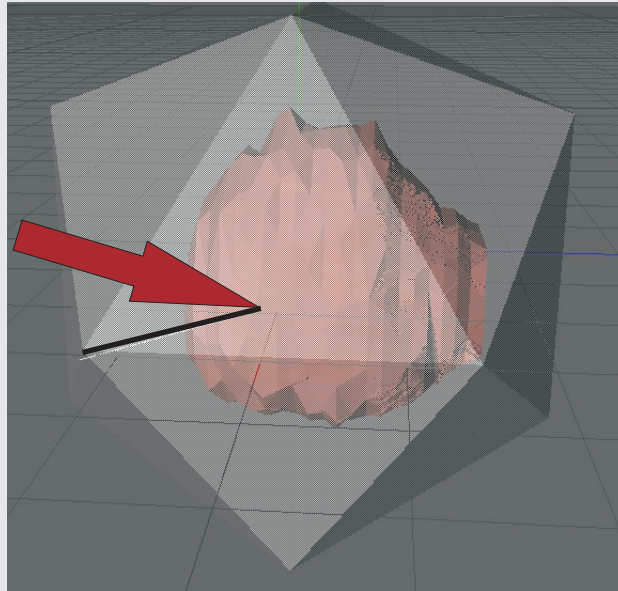


spine

kidney

# Forecast

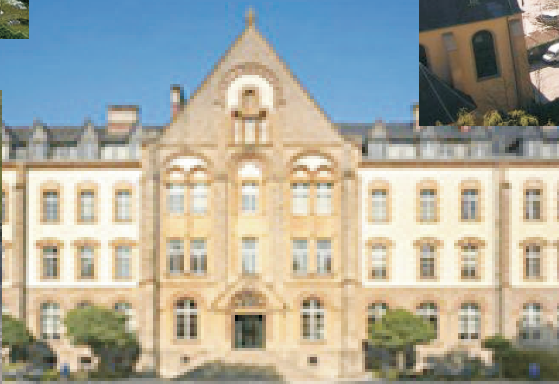
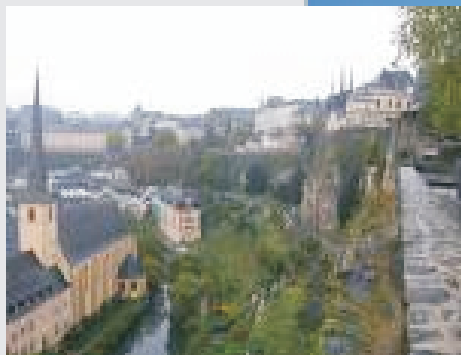
Determining of three dimensional landmarks



**Aim:  $n > 100$**



Faculté de Droit,  
d'Économie  
et de Finance



Merci vielmals !

# Application of statistical shape analysis to the classification of renal tumours appearing in early childhood



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