Applying Shape Analysis on two dimensional objects in medicine: Differentiation of tumours in early childhood

Stefan Markus Giebel, Jang Schiltz[1], Jens-Peter Schenk[2]

1 Summary

We describe one applications of statistical shape analysis. For the differentiation of the different kidney tumours appearing in early childhood we use shape analysis of two-dimensional MRI images. A descriptive approach and a test to differentiate tumours by the distance to the mean shape are shown.

2 Introduction

In a wide variety of disciplines it is of great practical importance to measure, describe and compare the shapes of objects. In general terms, the shape of an object, data set, or image can be defined as the total of all information that is invariant under translations, rotation and isotropic rescaling. The field of shape analysis involves hence methods for the study of the shape of objects where location, rotation and scale can be removed. The two- or more dimensional objects are summarized according to key points called landmarks. This approach provides an objective methodology for classification whereas even today in many applications the decision for classifying according to the appearance seems at most intuitive.
Statistical shape analysis is concerned with methodology for analyzing shapes in the presence of randomness. It is a mathematical procedure to get the information of two- or more dimensional objects with a possible correction of size and position of the object. So objects with different size and/or position can be compared with each other and classified. To get the shape of an object without information about position and size, centralisation and standardisation procedures are used in some metric space.
Interest in shape analysis began in 1977. D.G. Kendall (1977) published a note in which he introduced a new representation of shapes as elements of complex projective spaces. K.V. Mardia (1977) on the other hand investigated the distribution of the shapes of triangles generated by certain point processes, and in particular considered whether towns in a plain are spread regularly with equal distances between neighbouring towns. The full details of this elegant theory which contains interesting areas of research for both probabilists and statisticians where published by D. Kendall (1984) and F. Bookstein (1986). The details

[1] Université du Luxembourg, Luxembourg
[2] Paediatric Radiology, University of Heidelberg, Germany

of the theory and further developments can be found in the textbooks by C.G. Small (1996) and I.L. Dryden & K.V. Mardia (1998).
We present one applications of statistical shape analysis: the classification of renal tumours.

3 Renal tumours in early childhood

In the special case of oncology there is no theoretical medical reason to select a specific group of landmarks for differentiation. All landmarks in this research have thus to be selected by an explorative procedure.
Nephroblastoma (Wilms? tumour) is the typical tumour of the kidneys appearing in childhood. Therapy is organized in therapy-optimizing studies of the Society of Paediatric Oncology and Haematology (SIOP). Indication of preoperative chemotherapy is based on radiological findings. The preferred radiological method is sonography and MRI. Both methods avoid radiation exposure, which is of great importance in childhood. Preoperative chemotherapy is performed without prior biopsy (Schenk 2006).
Information of the images of magnetic resonance tomography, especially the renal origin of a tumor and the mass effect with displacement of other organs, is needed for diagnosis. Next to nephroblastomas other tumors of the retro peritoneum exist, which are difficult to differentiate (Schenk, 2008). Renal tumours in childhood are classified in three stages of malignancy (I, II, III). Typical Wilms tumours mostly belong in stage II. In stage II different subtypes of nephroblastoma tissue exist (Graf 2003).
In our sample of tumours in childhood, there are four different types of tumours: nephroblastoma, neuroblastoma, clear cell carcinoma, and renal cell carcinoma. Renal cell carcinomas are very rare in childhood. They represent the typical tumours of adult patients. They have no high sensitivity for chemotherapy. Clear cell sarcomas are very rare in childhood and are characterized by high malignancy. Neuroblastoma is the main differential diagnosis to nephroblastoma. It is the typical tumour of the sympathetic nervous system and suprarenal glands. Infiltration of the kidney is possible. The tumour grows with encasement of vessels. Because of the high importance of radiological diagnosis for therapy, it is of great interest to find markers for a good differentiation of these tumours.

4 Sample

The research sample in frontal perspective consists of 24 cases of tumours: 18 nephroblastoma, 3 neuroblastoma, 2 clear cell carcinoma and 1 renal cell carcinoma. In transversal perspective we have 15 cases of tumours: 8 nephroblastoma, 3 neuroblastoma, 2 clear cell carcinoma and 2 renal cell carcinoma. Main diagnostic tools are sonography, CT and MRI.

Because MRI has no radiation exposure it is the preferred radiological method. Using the images in frontal and transversal direction two three dimensional objects are constructed.
Then the mass point of the three dimensional object at all is calculated for every tumour to make them comparable. The real tumours distinguish itself by their position in the three dimensional body. Since we can use only one two-dimensional image of all the existing images of a patient we have to assure that a similar image can be found in the data of the other patients.
By the use of statistical shape analysis, the object is hence reduced to two dimensions, standardised and centred.

5 Results of shape analysis

After the objects are centred and standardises the mean shape of nephroblastoma is calculated and also the distance of all nephroblastomas to their mean shape.
The distance of every nephroblastoma to the mean shape is calculated by the Euclidean norm. Every tumour gets a rank by the distance to the mean shape. High rank means a high distance to the mean shape.

Tabelle 1: Distances of the nephroblastoma Wilms-tumours to the mean shape in frontal perspective

patient		distance	
No.	diagnosis	d_f	$rank_{Wilms}$
No.1	u.	0.0849	3
No.2	IId	0.1009	6
No.3	IIc	0.2260	18
No.4	IIIa	0.0968	5
No.5	IIa	0.1567	13
No.6	IIb	0.1113	8
No.7	IId	0.1940	17
No.8	IId	0.1448	12
No.9	IId	0.1854	16
No.10	IIc	0.1290	11
No.11	IIb	0.1834	15
No.12	IIa	0.0772	2
No.13	IIc	0.0916	4
No.14	IIc	0.1058	7
No.15	IIc	0.1126	9
No.16	n.b.	0.0541	1
No.17	IIa	0.1178	10
No.18	IIc	0.1754	14

I,II,III:class of risk of Wilms-tumours; a,b,c: types depending on classu.:unknown diagnosis

The arithmetic mean of distance in frontal perspective is $\overline{d} = 0.1304$.

Tabelle 2: Distances of the nephroblastoma Wilms-tumours to the mean shape in transversal perspective

patient		distance	
No.	diagnosis	d_t	$rank_{Wilms}$
No.8	IId	0.0998	3
No.12	IIa	0.0966	2
No.15	IIc	0.0772	1
No.6	IIb	0.1164	4
No.5	IIa	0.1791	8
No.4	IIa	0.1752	7
No.2	IId	0.1112	3
No.9	IId	0.1414	5

I,II,III:class of risk of Wilms-tumours; a,b,c: types depending on classu.:unknown diagnosis

The arithmetic mean of distance in transversal perspective is $\overline{d} = 0.1239$.

Tabelle 3: Distances of the nephroblastoma Wilms-tumours to the mean shape in frontal perspective

patient		distance	
No.	diagnosis	$d_{all} = d_f + dt$	$rank_{Wilms}$
No.8	IId	0.2446	5
No.12	IIa	0.1738	1
No.15	IIc	0.1898	2
No.6	IIb	0.2277	4
No.5	IIa	0.3358	8
No.4	IIIa	0.2734	6
No.2	IId	0.2121	3
No.9	IId	0.3268	7

I,II,III:class of risk of Wilms-tumours; a,b,c: types depending on classu.:unknown diagnosis

The arithmetic mean of distance is $\overline{d} = 0.248$.

To test the mean shape for differentiation the tumours we are using the test of

Ziezold(1994) [3].

Test of Ziezold (1994):

1. step: set of objects o
There is one set $M = o_1, \ldots, o_N$ can be divided in two subsets: objects with the characteristic A $A^{sample} = \{o_1, \ldots, o_n\} = \{a_1, \ldots, a_n\}$ and objects with the characteristic B $B^{sample} = \{o_{n+1}, \ldots, o_N\} = \{b_1, \ldots, b_{N-n}\}$.
Subset A is an independent realisation of distribution P and subset B is an independent realisation of distribution Q.
Hypothesis:
$H_0 : P = Q$

Alternative:
$H_1 : P \neq Q$

Set α as niveau of significance. If the probability for H_0 is smaller, we neglect H_0 and assume H_1.

2.step: Calculating the mean shape
The mean shape is calculated by the algorithm of Ziezold (1994):

m_0 ist the mean shape of the subset A.

3.Schritt: Calculating the u-value u-value:

$u_0 = \sum_{j=1}^{n} card(b_k : d(b_k, m_0) < d(a_j, m_0))$

4.step: Calculating all possibilities of dividing the set in two subset with the same proportion.

5.step: Comparing the u_0-value to all possible u-values. Calculate the rank. Small u-values means a small rank.

6.step: Calculate p for H_0 $p_{r=i} = \frac{1}{\binom{N}{n}}$ for $i = 1, \ldots, \binom{N}{n}$. r is the rank and we assume for the rank a rectangular distribution. The result should be proved also in the direction of the subset B.

[3] Ziezold, H., "Mean Figure and Mean Shapes applied to biological figure and Shape distributions in the plane", Biometrical Journal 36, 1994; S.491-510

For the types of tissue we have 15 Wilms-tumours with diagnosis:

Tabelle 4: Differentiation of types of Wilms-tumours in stage II

sets		Types					
Typ 1	Typ 2	u_0	$m_=$	$m_<$	$p - Intervall$	k	$\binom{15}{k}$
$Typ\ a$	$\overline{Typ\ a}$	0	57	0	$[0.002, 0.125]$	3	455
$\overline{Typ\ a}$	$Typ\ a$	21	14	338	$[0.745, 0.774]$	12	455
$Typ\ b$	$\overline{Typ\ b}$	2	22	64	$[0.619, 0.819]$	2	105
$\overline{Typ\ b}$	$Typ\ b$	9	5	37	$[0.362, 0.409]$	13	105
$Typ\ c$	$\overline{Typ\ c}$	6	17	431	$[0.086, 0.090]$	6	5005
$\overline{Typ\ c}$	$Typ\ c$	14	155	780	$[0.156, 0.187]$	9	5005
$Typ\ d$	$\overline{Typ\ d}$	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 permutations with the same u-value; $m_<$: number of permutations with a smaller u-value

Only Typ c shows a possibility for differentiation in both direction.Before using the test of Ziezold we look on the distances of Non-Wilms-tumours to the mean shape of Wilms-tumours. The rank is calculated in the group of Wilms-tumours.

Tabelle 5: Distances of Non-Wilms-tumours to Wilms-tumours

patient		distance					
Nr.	kind of tumour	d_f	$rank_{19}$	d_t	$rank_9$	$d_f + d_t$	$rank_9$
No.19	clear cell sarcoma	0.2324	19	0.1182	6	0.3506	9
No.20	clear cell sarcoma	0.1605	15	0.1356	6	0.2961	7
No.21	neuroblastoma	0.2969	19	0.1275	6	0.4244	9
No.22	neuroblastoma	0.1775	16	0.4151	9	0.5926	9
No.23	renal cell carcinoma	0.1082	8	0.0834	2	0.1916	9
No.24	neuroblastoma	0.1227	11	0.1793	9	0.3020	7
No.25	renal cell carcinoma	n.a.	n.a.	0.0822	2	n.a.	n.a.

n.a.: not avaliable

rank of one Non-Wilms-tumour in the group of Wilms-tumour

It can be shown that the renal cell carcinoma are very difficult to differentiate them from Wilms-tumour. They are very near to the mean shape of Wilms-tumours. Neuroblastoma and clear cell carcinoma have a greater distance to the mean shape of Wilms-tumours than renal cell carcinoma.To proove the statement we use the test of Ziezold (1994). Because the number of cases in transversal perspective is very small we use only the frontal perspective.
For the frontal perspective:

Tabelle 6: Result with / without renal cell carcinoma

sets		Differentiation						
kind of tumour 1	kind of tumour 2	u_0	$m_=$	$m_<$	$p-Intervall$	k	n	$\binom{n}{k}$
Wilms	"Non-Wilms"	28	1345	9375	$[0.070, 0.080]$	18	24	134596
"Non-Wilms"	Wilms	54	2345	105663	$[0.785, 0.802]$	6	24	134596
Wilms	N1+K	17	210	921	$[0.027, 0.034]$	23	18	33649
N1+ K	Wilms	43	704	26118	$[0.776, 0.797]$	23	5	33649

N1: neuroblastoma; K: clear cell sarcoma; $m_=$: number of permutations with the same u-value; $m_<$: number of cases with a smaller u-value

In the direction of the mean shape of Wilms-tumour the kind of tumours can be differentiated. If the procedure to differentiate after standardisation and centring is usefull, we have to look on different possible procedures.

Tabelle 7: Differentiation of Wilms- to Non-Wilms in frontal perspective

Characteristic		Differentiation of the kind of tumours						
characterustic	Mathematical procedure	u_0	$m_=$	$m_<$	$p-Intervall$	k	n	$\binom{n}{k}$
shape I	"2D centred" + "standardised"	28	1345	9375	$[0.070, 0.080]$	18	24	134596
shape II	"3D centred" + "standardised"	37	2575	27506	$[0.2044, 0.2235]$	18	24	134596
figure	"2D centred"	43	2971	37787	$[0.2808, 0.3028]$	18	24	134596
original	"3D centred"	45	3125	44495	$[0.3306, 0.3538]$	18	24	134596

The u_0-value and the p-value are smallest in the case of "2D centred" + "standardised" the procedure and so the procedure is useful for differentiation. The group of Non-Wilms-tumours is heterogeneous. That's why the differentiation for every kind of tumours is of further interest.

Tabelle 8: Differentiation from all kind of tumours to each other

sets		Differentiation						
kind of tumour 1	kind of tumour 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

N1: neuroblastoma; N2: renal cell carcinoma; K: clear cell sarcoma; $m_=$: number of permutations with the same u-value; $m_<$: number of permutations with a smaller u-value

According to the table clear cell sarcoma can be differentiated in both direction and Wilms-tumours can be differentiated from neuroblastoma.

6 Conclusion

Shape analysis can be a solution in decision processes on two dimensional data. Especially in medicine shape analysis is an objective tool for differentiation.
More data are needed to prove the differentiation. In further research three dimensional landmarks of tumours are used. Three dimensional landmarks are taken as cut points between the three dimensional surface of the tumour and the line between mass point and an edge of a platonic object. Also a test for selection the relevant configuration of landmarks for differentiation has to be developed.

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