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Poluautomatska procjena stupnja sazrijevanja vratnih kralježaka iz radiografskih kefalograma i klasteriranje na temelju centroida

Semi-automatic Assessment of Cervical Vertebral Maturation Stages using Cephalograph Images and Centroid-based Clustering

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Sažetak
Korištenjem radiograma istraživala se učinkovitost različitih numeričkih tehnika za poluautomatske procjene stupnja sazrijevanja vratnih kralježaka (CVM). **Metode:** Kefalogrami 211 pacijenata snimljeni su i spremljeni u digitalnom obliku. Nakon toga su, s pomoću posebno razvijenog softvera i tih pohranjenih radiograma, specijalisti ortodoncije označili i mjerili za svakog pacijenta nekoliko karakterističnih kefalometrijskih obilježja. Rezultati su bili potrebni za automatsko određivanje stupnja sazrijevanja vratnih kralježaka s nekoliko numeričkih tehnika, među kojima **K** znači klasteriranje (grupiranje), a **Fuzzy C** – dusteriranje (rasipanje). Rezultati su uspoređeni s podacima koje su dobili specijalisti. **Rezultati:** Najbolji rezultati dobiveni su korištenjem Fuzzy C rasipanja. Točna ocjena stupnja CVM-a iznosila je oko 70 posto, a procjena klase bila je viša od 99 posto. **Zaključak:** Eksperimentalni rezultati pokazuju da se može razviti potpuno automatizirani sustav za procjenu i predviđanje stupnjeva CVM-a, premda još treba riješiti manje teškoće prije primjene u kliničkoj praksi.

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Ključne riječi
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Uvod

Tijekom razvoja svaka ljudska kost prolazi niz faza. U ortodonciji i facijalnoj ortopediji faza mandibularnog rasta važna je za postavljanje dijagnoze, za terapijske ciljeve u planiranju terapije i moguće rezultate ortodontskog liječenja. Slijed promjena za pojedine kosti poznat je kod svake osobe, ali njihovo sazrijevanje varira i usko je povezano s dobi pacijenta (1).

Mora se uzeti u obzir to da svaka osoba ima vlastiti biološki sat (2), pa se kronološka ili *stvarna dob* često ne podudara s onom fiziološkom. Fiziološka dob koncept je razvijen kako bi se uzele u obzir velike razvojne razlike među djecom iste kronološke dobi. Ona je zapravo zapis brzine sazrijevanja koju se može procjenjivati kao somatsku, spolnu, skeletalnu i zubnu (3 4). Fiziološka dob opisuje stupnjeve sazrije-

Introduction

During growth, every human bone undergoes a series of development stages. In orthodontics and facial orthopedics, the stages of mandibular growth have a considerable influence on the diagnosis, treatment goals, treatment planning, and final outcome of orthodontic treatment. The sequence of changes is relatively constant for a given bone in every person, but the timing of these changes varies, and it is closely related to the developmental age of the patient (1).

Considering that every person has his or her own biological cloc (2), the chronological age (or the "real" age) often does not match its developmental or physiological age. The physiological age is a concept which was developed to take into account considerable temporal variations in development among children of the same chronological age. Physvanja kostiju, ili skeletalnu dob kostiju. Zbog individualnih varijacija u sazrijevanju, trajanju i brzini rasta, procjena skeletalne dobi prijeko je potrebna u sastavljanju plana ortodontske terapije. Tako je, primjerice, najveći učinak funkcionalne ortopedije čeljusti uspoređivan s rastom u razdoblju puberteta (5).

U literaturi je opisano nekoliko načina procjene skeletalne dobi. Jedna od standardnih jest radiogram šake (6, 7). Kako bi se što je više moguće smanjilo dodatno izlaganje djece rendgenskim ili X- zrakama, razvijena je nova procjena zrelosti kostiju – metoda sazrijevanja vratnih kralježaka (CVM) (2, 5, 8 – 10). Na taj se način stupanj zrelosti vratnih kralježaka može odrediti na lateralnim kefalogramima. Stupanj zrelosti kralježaka olakšava procjenu fiziološke dobi pacijenta.

Ovisno o autorima i klasifikacijama postoji pet (4) ili šest (11) stupnjeva CVM-a. Obično se određuje na radiogramima prema obliku trećeg i četvrtog vratnog kralješka, a imaju tipične geometrijske karakteristike koje olakšavaju razlikovanje. Premda je pouzdanost i vrijednost te metode statistički dokazana kao prihvatljiva (12), neki autori smatraju da se moraju razmotriti i mnogi drugi indikatori rasta pri procjeni skeletalnog sazrijevanja adolescenata (13). Kako bi se smanjile složenost i subjektivnost, a povećala pouzdanost procjene skeletalne dobi, posljednjih je godina predloženo nekoliko novih automatiziranih metoda (ABAA) (14, 15).

Baptista i suradnici (10) nedavno su se koristili CVM-klasifikacijom kompjutoriziranim uzorkom. Njihov pristup bio je nešto drugačiji jer su se služili Bayesianovom teorijom odluke. Rezultati su bili slični rezultatima u ovom istraživanju i pokazali su da metoda poluautomatizirane klasifikacije može pomoći ortodontu u identifikaciji stupnja CVM-a te da pridonosi većoj dijagnostičkoj točnosti i boljem ortodontskom planu liječenja. No, ipak su potrebna dodatna istraživanja prije nego što se primijeni u kliničkoj praksi.

U ovom članku opisane su različite numeričke tehnike za poluautomatsko određivanje CVM-stupnja korištenjem digitalnih kefalograma.

Budući da se u svakodnevnom životu često koristimo *mutnom logikom*, bilo je normalno da se razvije takav pokazatelj i za procjenu CVM-a. Rezultati pokazuju da taj pristup omogućuje zadovoljavajuće rezultate te da se stadiji CVM-a mogu, umjesto geometrijski, analizirati i numerički.

iological age can be viewed as a registry of the rate of progress toward maturity that can be estimated, among others, by somatic, sexual, skeletal, and dental maturity (3,4). The physiological age describes the maturation status, or the skeletal age of a bone.

Because of the individual variations in timing, duration and speed of growth, skeletal age assessment is essential in orthodontic treatment planning. For example, the greatest response to functional jaw orthopedics tends to occur during the circumpubertal growth acceleration period (5).

Several methods used for skeletal bone age assessment have been described in literature. One of the early methods was using hand and wrist radiograph. In order to minimize an additional X-ray exposure for children, a new method for assessment of bone maturity - Cervical Vertebral Maturation method (CVM) was popularized (6-10) . Using the CVM method, developmental stages of cervical vertebrae can be determined from the lateral cephalographs. This, in turn, facilitates the assessment of the physiological age of the patient.

There are five (4) or six (11) CVM stages, depending on the authors and classification. The CVM stages are determined usually by describing the shapes of the third and the fourth cervical vertebrae on the radiographic image. The CVM stages follow typical geometrical characteristics that facilitate the differentiation between them.

Even though the validity and reliability of the CVM method was shown to be statistically acceptable (12), some authors suggest that other growth indicators should be taken into consideration in assessing levels of the adolescent skeletal maturation (13).

In order to reduce the complexity and subjectivity and, at the same time, to increase the reliability of skeletal bone age assessment, a variety of new methods for automatic bone age assessment (ABAA) have been proposed over recent years (14,15).

Baptista et al. (10) also recently used computer pattern classification for CVM classification. Their approach is somewhat different, because they used Bayesian decision theory for classification. The results of their study are quite similar to our results, showing that proposed semi-automated classification method can successfully assist orthodontists in identifying the stage of CVM, and thus contributing to a greater diagnostic accuracy and better orthodontic treatment planning. However, it is understood that more studies are needed before the methods can be routinely implemented in the clinical practice.

This paper describes various numerical techniques used for the semi-automatic assessment process of the CVM class, derived from digitized cephalograph images. Considering that the 'fuzzy reasoning' is used in everyday life, it was natural to develop a fuzzy-based logic indicator for CVM class assessment. The results show that this approach gives satisfactory results, and indicate that CVM classes, instead of using geometrical, could be analyzed using the ordinary numerical features.

Materijali i metode

U ovom istraživanju korištena su 102 kefalograma muškaraca i 109 kefalograma žena (ukupno 211) u dobi između 8 i 16 godina. Slike su pohranjerne u digitalnom obliku u posebnoj aplikaciji. Specijalisti ortodoncije su na njima označili karakteristične kefalometrijske točke. Mjerenja su se obavljala tehnikom numeričke klasifikacije temeljene na klasteriranju i korištene za testiranje korelacije između kefalometrijskih parametara i procijenjenog stupnja CVM-a.

Razvijeni softverski program i grafičko sučelje

Kako bi se izmjerile karakteristične udaljenosti na radiografskim slikama, bilo je potrebno razviti posebnu aplikaciju (na slici 1. vidi se njezin početni izgled). Na taj se način omogućuje unošenje radiograma i ručno označavanje karakterističnih kefalometrijskih točaka. Slika se premjerava u postupku uvođenja, tako da se svaka udaljenost mjeri u milimetrima. Kako slike mogu potjecati iz različitih izvora, poput digitalnih aparata ili skenera, sve moguće distorzije uklanjaju se bilinearnom projektivnom transformacijom i posebnim oznakama na rubu. Testirana je točnost aplikacije te je ustanovljeno da pogreška iznosi manje od 0,1 posto. Točnost mjerenja ovisi isključivo o korisniku ili koliko točno korisnik označava točke koje ga zanimaju. Negativan utjecaj na mjerenje smanjen je uvijek mogućim povećavanjem slike. Aplikacija je zatim proširena tako da omogućuje izračun drugih kefalometrijskih mjera koje se mogu eksportirati i spremiti u posebne tablične datoteke. Na temelju pojedinih zuba mogu se odrediti i kronološka i zubna dob. Funkcionalnost za određivanje stadija CVM-a analiziranih pacijenata temelji se na obavljenim mjerenjima i poslije će biti detaljnije opisana. Algoritmi koji omogućuju tu funkciju potanko će biti opisani u sljedećem poglavlju. Jedna od glavnih teškoća kod te aplikacije jest oslanjanje na oznake koje se postavljaju za karakteristične točke interesa jer povećavaju mogućnost pogrešaka tijekom mjerenja. U ovoj verziji softvera, zbog posebnosti radiograma (male varijacije sive boje, što znatno otežava segmentaciju i jako su zahtjevne za izračunavanje) (16, 17), nije primijenjeno potpuno automatizirano mjerenje kefalometrijskih obilježja.

Kefalometrijske točke CVM-a

Metoda sazrijevanja vratnih kralježaka (CVM) omogućuje određivanje zubne dobi pacijenata. Temelji se na procjeni razvojnih stadija vratnih kralježaka na lateralnim kefalogramima. Kako bi se odredio stupanj CVM-a, različiti tipovi vratnih kralježaka klasificiraju se u šest skupina ili razreda (slika 2.), ili u pet razreda (klinička ispitivanja pokazuju da bi se prva dva stupnja trebala spojiti).

Kao što se vidi na slici 2. i iz istraživanja Bacettija i njegovih suradnika, prva dva stupnja jako su slična te smo se zato u ovom istraživanju koristili s pet stupnjeva sazrijevanja (CVM I. do CVM V.). Evo njihovih opisa:

– *CVMS I.* (CS 1 i CS 2): tijela C3 (treći kralježak) i C4 (četvrti kralježak) trapezoidnog su oblika;

Material and Methods

For this study, cephalographs of 102 male and 109 female subjects (total of 211 films), aged from 8 to 16 years, were obtained. These images were then stored in a digital form and the resulting data imported into a specially developed application. Trained orthodontists marked characteristic cephalometric points on the cephalographs. The measurements were used as inputs to clustering based numerical classification techniques, and then used to investigate the correlation between the cephalometric parameters and the evaluated CVM class.

Developed software program and graphical interface

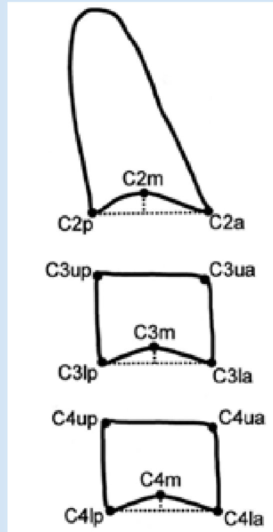
In order to measure the characteristic distances on a radiographic image, a special application soft-ware needed to be developed. Its screenshot is given in Figure 1. The application allows importing a radiographic image, and manual labeling of all the characteristic cephalometric points. The image is prescaled during the import phase, so that every distance is expressed in millimeters. Because the images may come from different sources, such as a digital camera or scanner, distortions are eliminated by using bilinear projective transformation, and by using special markers on the image frame. The accuracy of the application was tested, and it was shown that the measurement error was less than 0.1%. The accuracy of the measurements only depends on the user, or how accurately the user marks the points of interest. This effect is reduced by allowing the user to easily zoom the image at any time. This application is further enhanced by allowing other cephalometric measurements to be made. It also allows exporting and storing these measurements into a spreadsheet file. It can additionally determine chronological and dental age based on the development of certain teeth on the measurements made. The algorithms behind this feature are described in details in the following sections.

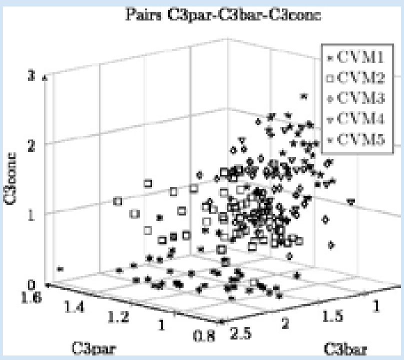
One of the main drawbacks of this application is that it relies on the user to mark the characteristic points, which increases the probability of measurement errors. Because of the specific features of the radiographic images (very low grey level variation which makes the segmentation difficult and computationally intensive and challenging to perform), (16,17), fully automatic measurements of cephalometric parameters [i.e. the complete cephalometric analysis] are not implemented in this version of the software.

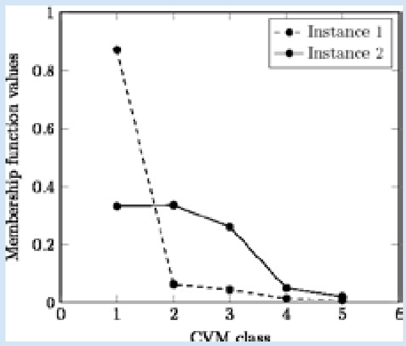
CVM cephalometric landmarks

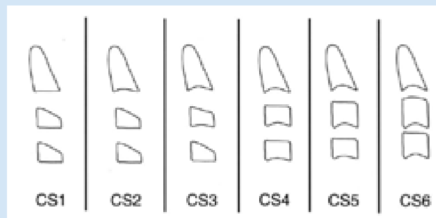
Cervical Vertebral Maturation method allows determination of the dental age of the patient. It is based on the assessment of the developmental stage of the cervical vertebrae from a standardized lateral cephalograph [*norma lateralis*]. In order to determine the stage of the CVM, different types of cervical vertebrae shapes are classified into groups or classes (CVM classes). According to Bacetti et al. [5], CVM stages could be classified into 6 classes (as shown in Figure 2), or into 5 classes (multiple clinical studies show that the first two classes could be merged).

It can be seen in Figure 2, and in the study of Bacetti et al., that the first two classes are very similar, so in this paper five maturation stages (CVM I to CVM V) are used:









Slika 1. Grafičko sučelje programa za kefalometrijsku analizu
Figure 1 Graphical interface of the cephalometric analysis program
Slika 2. Shematski prikaz stupnjeva maturacije vratnih kralježaka (prema Baccettiju i suradnicima)(5)
Figure 2 Schematic representation of the stages of cervical vertebrae (according to Baccetti et al. [5])
Slika 3. Kefalometrijske oznake za kvantitativnu analizu morfoloških karakteristika tijela kralježaka (5)
Figure 3 Cephalometric landmarks for the quantitative analysis of the morphologic characteristics of the vertebral bodies [5]
Slika 4. Primjer *mutne*/fuzzy funkcije pripadanja u različitim slučajevima
Figure 4 Example of fuzzy membership functions of different instances
Slika 5. Disperzija stupnjeva CVM-a
Figure 5 Dispersion of CVM classes

– *CVMS II.* (CS 3): uočava se konkavnost na donjem rubu C3, tijela C3 i C4 prema obliku su trapezoidna ili pravokutno vodoravna;
– *CVMS III.* (CS 4): uočava se konkavnost na donjem rubu C3 i C4, tijela C3 i C4 prema obliku su pravokutno vodoravna;
– *CVMS IV.* (CS 5): uočava se konkavnost na donjem rubu C3 i C4, ili C3 ili C4 prema obliku su pravokutni;
– *CVMS V.* (CS 6): uočava se konkavnost na donjem rubu C3 i C4, ili C3 ili C4 prema obliku su pravokutno vodoravni.

Oblik tijela kralježaka klasificiran je kao *trapezoidni* (gornji rub je nagnut od straga prema sprijeda), *pravokutno vodoravni* (jednaka je stražnja i prednja visina kralježaka; gornji i donji rubovi duži su od prednjih i stražnjih), *kvadratni* (stražnji, prednji, gornji i donji rubovi su jednaki), *pravokutno vertikalni* (stražnji i prednji rubovi duži su nego gornji i donji).

Baccetti i suradnici predložili su kvalitativnu analizu svojstava koja bi se mogla iskoristiti za učinkovito razlikovanje među stupnjevima CVM-a (kefalometrijska analiza). Karakteristična obilježja vratnih kralježaka (C3-up, C3-ua, C3-

- *CVMS I* (CS1 and CS2): The bodies of C3 (third vertebra) and C4 (fourth vertebra) are trapezoidal in shape.
- *CVMS II* (CS3): Presence of concavities at lower border of C3, and bodies of C3 and C4 are trapezoidal or rectangular horizontal in shape.
- *CVMS III* (CS4): Presence of concavity at the lower border of C3 and C4, and bodies of C3 and C4 are rectangular horizontal in shape.
- *CVMS IV* (CS5): Presence of concavity at the lower border of C3 and C4. At least one of C3 and C4 is square in shape.
- *CVMS V* (CS6): Presence of concavity at the lower border of C3 and C4. At least one of C3 and C4 is rectangular vertical.

The shape of the body of the vertebrae is classified as: *trapezoidal* (the superior border is tapered from posterior to anterior), *rectangular horizontal* (the heights of the posterior and anterior borders are equal; the superior and inferior borders are longer than anterior and posterior borders), *squared* (the posterior, superior, anterior and inferior borders are equal), and *rectangular vertical* (the posterior and anterior borders are longer than the superior and inferior borders).

lp. C3-m, C3-la, C4-up,C4-ua, C4-lp, C4-m, C4-la) nalaze se na slici 3. S pomoću tih obilježja mogu se obaviti sljedeća mjerenja:

- *C3-conc:* dubina konkaviteta na donjem rubu C3;
- *C4-conc:* dubina konkaviteta na donjem rubu C4;
- *C3-bar:* omjer između dužine baze i prednje visine tijela C3;
- *C3-par:* omjer između stražnje i prednje visine tijela C3;
- *C4-bar:* omjer između duljine baze i prednje visine tijela C4;
- *C4-par:* omjer između stražnje i prednje visine tijela C4.

Očito je da parametri C3-conc i C4-conc opisuju konkavitet donjeg ruba kralježaka, C3-par i C4-par rabe se za određivanje jesu li kralješci trapezoidnog oblika, a C3-bar i C4-bar služe za opisivanje kvadratnog ili pravokutnog oblika. U tablici 1. predstavljen je kvalitativni opis kefalometrijskih mjera za određeni stupanj CVM-a prema Baccettiju (5).

Baccetti suggested a qualitative analysis of parameters which could be used for effective discrimination between CVM classes (cephalometric analysis). Characteristic landmarks of cervical vertebrae (C3up, C3ua, C3lp. C3m, C3la, C4up,C4ua, C4lp, C4m, C4la) are shown in Figure 3. With the aid of these landmarks, the following measurements were performed:

- *C3conc:* Measure of the concavity depth at the lower border of C3,
- *C4conc:* Measure of the concavity depth at the lower border of C4,
- *C3bar:* Ratio between the length of the base and the anterior height of the body of C3,
- *C3par:* Ratio between the posterior and the anterior height of the body of C3,
- *C4bar:* Ratio between the length of the base and the anterior height of the body of C4,
- *C4par:* Ratio between the posterior and the anterior height of the body of C4.

Obviously, the C3conc and C4conc parameters describe the concavity of the lower border of the vertebrae, C3par and C4par are used to determine if a vertebra has trapezoidal shape, while C3bar and C4bar are used for describing if a shape is rectangular or squared. Table I is formed according to the quantitative description of the cephalometric measures for a given CVM class from Baccetti (5).

Tablica 1. Centroidni vektori stupnja prema mjerenjima Baccettija (5)
Table 1 Class centroid vectors formed according to Baccetti (5) measurements

Class	C3conc	C4conc	C3par	C3bar	C4par	C4bar
I	0.36	0.12	1.26	1.77	1.25	1.71
II	0.95	0.31	1.16	1.61	1.15	1.59
III	1.36	1.07	0.98	1.39	1.01	1.36
IV	1.85	1.77	0.98	1.2	1.01	1.19
V	2.4	2.28	0.98	1.03	0.97	1.04

Mjerenje učinkovitosti

Kako bi se procijenili rezultati algoritama za svakog pacijenta, kao polazna točka rabio se stupanj CVM-a koji su odredili stručnjaci.

Tri parametra definirana su kao učinak mjerenja:

- *COIN-0* – postotak koincidencije koji je ustanovio specijalist i stupanj određen algoritmom;
- *COIN-1* – postotak koincidencije koji je ustanovio specijalist i stupanj određen algoritmom, ali uključeni su i slučajevi kod kojih su razlike samo jedan stupanj (primjerice, procjena specijalista je CVM III., a softvera CMV IV.). Dokazano je da je u nekim slučajevima teško razlikovati dvije susjedne klase/stupnja maturacije skeletalnih kostiju, pa tako mala razlika nije klinički relevantna (2, 10).
- *COIN-F* – postotak slučajeva koje su specijalisti ustanovili kao točne i u tom stupnju, prema nalazima primijenjenog algoritma, imaju funkciju rasapa (fuzzy membership) veću od 30 posto.

Performance measures

In order to evaluate the results of the algorithms, the CVM class determined by the experts for every instance was used as a reference. Three parameters are defined as performance measures:

- *COIN-0* - The percentage of coincidence of the class evaluated by experts and the algorithm class,
- *COIN-1* - The percentage of coincidence of the class evaluated by experts and the algorithm class, but including the instances where the classes differs by just one (eg. experts evaluate CVM III, but software evaluates CMV IV). It has been shown that in some cases it may be difficult to differentiate between two adjacent stages of skeletal bone maturation, so it may not be clinically relevant (2,10).
- *COIN-F* - The percentage of instances that the experts evaluated as correct and have the fuzzy membership function greater than 30% percent in that class according to the algorithm.

Tehnike klasificiranja

Tipičan pristup rješavanju problema klasifikacije jest kad su pojedini dijelovi skupa (primjerice, slike, mjerenja itd.) označeni numerički u obliku *opisnih vektora*. Opisni vektor mogao bi se objasniti kao skup brojeva koji opisuju određena svojstva nekog detalja. U ovom radu vektori ***X(i)***=*[C3-conc(i), C4-conc(i), C3-par(i), C3-bar(i), C4-par(i), C-4-bar(i)]* bili su opisni, gdje je ***i*** broj slučaja (pacijenta). Ako je zadatak klasificirati te vektore svojstava u ***m***-stupnjeve, tada se obično odabire reprezentativni (najkarakterističniji) vektor za opis pojedinog stupnja maturacije ***m***. Reprezentativni vektor obično se iz poznatog skupa podataka izvodi/pronalazi statistički. Ako je reprezentativni vektor stupnja maturacije poznat, slučajevi će se klasificirati u stupnjeve maturacije kod kojih je reprezentativni vektor *najsličniji* promatranom svojstvu.

Problem s takvom klasifikacijom jest da je svaki slučaj uvršten samo u jedan određeni stupanj, a klasifikacija uglavnom ovisi o odabranom reprezentativnom vektoru. To znači da će, ako su reprezentativni vektori različiti, i klasifikacija biti različita. Ti problemi bit će objašnjeni dalje u radu jer su u neposrednoj vezi s automatiziranom procjenom stupnja maturacije CVM-a.

Svrha ovog rada bila je riješiti problem klasifikacije ili predložiti stupanj CVM-a na temelju vrijednosti opisnog vektora. Pritom se nameću dva pitanja:

1. kako pronaći reprezentativni vektor za stupanj CVM-a (zvan centroid),
2. kako odlučiti kojem stupanju pripada pojedini slučaj, ili kako izračunati *sličnost* između vektora svojstva i reprezentativnog vektora stupnja?

Primijenjeni su ovi pristupi:

– kako bi se riješio prvi zadatak – pronašao centroid razreda, rabile su se četiri metode:
  o centroidi iz tablice 1.,
  o centroidi su pronađeni klasteriranjem K-srednjih vrijednosti,
  o centroidi su pronađeni klasteriranjem *mutnih* (fuzzy) C-srednjih vrijednosti,
  o centroidi su pronađeni modificiranim klasteriranjem *mutnih* (fuzzy) C-srednjih vrijednosti;
– kako bi se izračunale udaljenosti ili stupanj (zadatak klasifikacije) rabile su se metode:
  o standardna i težinska norma L1 (manhattanska ili udaljenost gradskog bloka),
  o standardna i težinska norma L2 (euklidska udaljenost),
  o standardna i težinska norma L∞ (maksimalna udaljenost),
  o funkcije pripadnosti (fuzzy C-sredine).

Zbog pojednostavljenja i jasnoće u ovom su radu izostavljene matematičke pojedinosti, a predstavljeni su i raspravljeni rezultati svih metoda.

Klasifikacija korištenjem tradicionalnog pristupa

U svakodnevnom životu, kao i u jednostavnoj matematici, razlike su obično jednodimenzionalne. Primjerice, kada se mjeri udaljenost između tri i deset centimetara na školskom

Classification techniques

Typical approach used when solving classification problems, is that instances from a given set (e.g. images, measurements etc.) are numerically described in form of the, so called, *feature vectors*. A feature vector could be explained as a set of numbers which describe certain features of an instance. In this paper, vectors *X(i)=[C3conc(i), C4conc(i), C3par(i), C3bar(i), C4par(i), C4bar(i)]* are used as feature vectors, where *i* is the instance (patient) number. If the task is to classify these feature vectors into *m* classes, then usually a representative (or most typical) vector for every class is chosen. The representative vector is usually derived using statistics on known datasets. Once the representative vector of a class is known, an instance will then be classified into the class for which the representative vector is the most 'similar' to the given feature vector.

The problem with this kind of classification is that a single instance is strictly classified into only one class, and the classification largely depends on the chosen representative vectors. This means that if the representative vectors were different, the classification would be different. These problems will be addressed further in the paper, because they are directly related to automatic CVM class assessment.

The task of this paper was to solve a classification problem, or to suggest a CVM class based on the value of the feature vector. Two subtasks are evident:

1. how to find the class representative vectors (called centroids),
2. how to decide to which class an instance belongs, or 'how to calculate the 'similarity' between the feature vectors and class representative vectors?'.

The following approaches were used:

- In order to solve the first task of finding class centroids, four methods were used:
  o Centroids from Table 1 are used,
  o Centroids are found using K-means clustering,
  o Centroids are found using Fuzzy C-means clustering,
  o Centroids are found using a modified version of Fuzzy C-means clustering.
- In order to calculate the distance, or membership of the class (classification task), the following methods were used:
  o Standard and weighted L1-norm (Manhattan or City block distance),
  o Standard and weighted L2-norm (Euclidean distance),
  o Standard and weighted L∞-norm (Maximum distance),
  o Using the membership functions (Fuzzy C-means).

In order to make this paper clearer, mathematical details will be omitted, while the results from all methods will be presented and discussed.

Classification using traditional approaches

In everyday life, and in simple mathematics, differences are usually one-dimensional. For example, when measuring the distance between the 3cm and 10cm mark on a ravnalu, jednostavno se oduzmu vrijednosti točaka i kao rezultat dobije se sedam centimetara, što znači da su te dvije točke toliko udaljene.

Nažalost, opisni vektori obično su višedimenzionalni. Za to je primjer klasifikacija stupnja CVM-a. To znači da nije jednostavno izračunati udaljenost između dviju točaka jer ne leže na određenoj liniji (opisujući njihovu vrijednost), nego negdje u višedimenzionalnom prostoru (vjerojatno većem od tri dimenzije).

Udaljenost dvaju opisnih vektora u višedimenzionalnom prostoru obično se opisuje p-normama (18). Kako bi se poboljšali COIN-0 i COIN-1, rabile su se težinske udaljenosti (norme) normalizirane *rasponskim* vektorom.

Pristup p-normi zahtijeva određivanje centroidnog vektora (reprezentativni uzorak stupnja). Metoda klasteriranja oko K-sredine omogućuje da se pronađe centroid stupnja istodobno s problemom klasifikacije. Metoda klasteriranja K-sredina jest način grupiranja kojim se opažene vrijednosti ***n*** slažu u klastere ***k*** u kojima svako opaženo svojstvo pripada klasteru s najbližom srednjom vrijednosti (19, 20). To znači da se, u ovom slučaju, opažanjem klasificira pet najrazličitijih mogućih stupnjeva i grupira oko zajedničke sredine (centroidnog vektora). Algoritam daje pet centroidnih vektora (tablica 2.) i trebali bi odgovarati stupnjevima CVM-a.

school ruler, we simply subtract the values of the points, and get 7cm as result, which means that these 2 points are 7cm apart.

Unfortunately, feature vectors are usually multidimensional. Classification of CVM classes is an example of a multidimensional classification. This means that the distance between two points is not simple to calculate, because the two points do not lie on one specific line (describing their value), but are somewhere in a multidimensional space (probably greater than commonly used 3-dimensional space).

The distance between two (feature) vectors in multidimensional space is typically calculated using p-norms[18] .

In order to improve COIN-0 and COIN-1 measures, weighted distances (norms) were used, normalized with a 'range' vector.

The p-norm approach requires that centroid vectors (class representatives) are already defined. The K-means clustering method allows us to find the centroids of the classes, and solve the classification problem at the same time. K-means clustering is a method of cluster analysis which aims to partition *n* observations into *k* clusters in which each observation belongs to the cluster with the nearest mean(19,20). It means that, in this case, the instances will be classified into 5 classes that are as different as possible, and will group around the common means (centroid vectors). This algorithm gives 5 centroid vectors (Table II), and CVM classes should correspond to them.

Tablica 2. Centroidni vektori stupnja prema klasteriranju K-sredina
Table 2 Class centroid vectors according to K-means clustering

Km Class	C3conc	C4conc	C3par	C3bar	C4par	C4bar
Class-1	0.1950	0.1011	1.2200	1.7992	1.1687	1.8168
Class-2	1.4078	0.1649	1.1725	1.5515	1.1249	1.6168
Class-3	0.9094	0.4038	1.1106	1.4581	1.0928	1.5271
Class-4	1.5613	0.9201	1.0949	1.1812	1.0948	1.2646
Class-5	2.1183	1.5042	1.0674	1.0411	1.0491	1.1101

Klasifikacija korištenjem algoritma mutne *C-sredine*

Ponekad se pojavljuju slučajevi poput onoga kada je jedan kralježak trapezoidni, a drugi kvadratni. Teško je dobiti oštru klasifikaciju jer prvi parametarski vektor obilježja upućuje na to da bi mogao biti prvog ili drugog stupnja, a drugi vektor upućuje na četvrti. To znači da je klasifikacija *mutna* i da odabrani stupnjevi (što god da jesu) nisu sigurni.

Čak i u stvarnom svijetu, ako postoji problem klasifikacije, više obilježja onogućuje pravilniju odluku, tako da je prirodno primijetiti da klasifikacija CVM-a ne treba biti oštra i da je bolje primijeniti više parametara. Metoda koja omogućuje *mutni* pristup jest metoda klasteriranja *mutnih* C-sredina (21 – 23). Za razliku od klasteriranja K-sredina koje definira pripadnost samo jednom stupnju, metoda *mutnih* C-sredina omogućuje uvrštavanje jednog obilježja u dva ili više klastera, uz određenu funkciju pripadnosti. *Mutna* pripadnost vrlo je jednostavna za razumijevanje jer tim se načinom razmišljanja svakodnevno koristimo. Primjerice *visok* je mutna mjera visine (ovisi o poimanju što je to *visok*), a toč-

Classification using Fuzzy C-means algorithm

Sometimes, cases such as the one where one vertebra is trapezoidal in shape, and the other is square, could arise. It is then difficult to obtain a strict classification; because the first feature vector parameter indicates it could be class I or II, while the second indicates it is class IV. This means that the classification is 'fuzzy', and that the selected class (whatever it is) has some degree of uncertainty.

Even in a real world classification problem, more features mean better decisions, so it is natural to observe that CVM classification should not be strict. The use of multiple parameters of classification is certainly better.

The method that allows a 'fuzzy' approach is the Fuzzy C-means (21-23) clustering method. Unlike the K-means clustering, which defines an instance to be a member of only one class, the Fuzzy C-means allows one instance to belong to two or more clusters, with a certain membership function. The Fuzzy membership is rather intuitive to understand, because everyone uses this kind of reasoning daily. For example, 'tall' is a fuzzy measure of height (it depends on the underna je mjera visine (190 cm). Korištenjem prije opisanog primjera CVM-klasifikacije, opaženo svojstvo moglo bi 40 posto pripadati stupnju II., 30 posto stupnju III. i 30 posto stupnju IV., što je uobičajeni način odlučivanja u svakodnevnom životu.

To je jasno pogledamo li sliku 4. koja predstavlja funkciju *mutne* pripadnosti za slučaj iz skupine podataka. Prvi slučaj bez dvojbe se ubraja u prvi klaster (CVM I. stupnja). Drugi slučaj pripada drugom klasteru, premda bi se mogao svrstati i u prvi ili treći, ako se uzmu u obzir dodatni podaci za specifične slučajeve (primjerice, kronološka dob pacijenta).

Korištenje *mutne* pripadnosti stupnja CVM-a gotovo je prirodno jer je i ljudski rast neprekinuti proces.

Klasifikacija korištenjem modificiranog mutnog *pristupa*

Tijekom eksperimenta pojavio se jedan problem. Opažaji u višedimenzionalnom prostoru imaju malo drugačiji trend grupiranja, a ne samo u predviđene stupnjeve CVM-a. Kako bi se zadržali stupnjevi iz literature, s pomoću modificiranog pristupa m*utnih* C-sredina pokušalo se opažanja grupirati u pet stupnjeva koji bi točnije odgovarali stupnjevima CVM-a. Centroidi stupnjeva prije toga definirani su primjenom dvaju pristupa:

– sva opažanja svrstana su u pet stupnjeva korištenjem svih šest parametara odvojeno i tada je agregacijom oblikovan centroid skupine; dobiveni centroidni vektori nalaze se u tablici 3.
– centroid je dobiven na temelju 50 posto svih mjerenja ortodonata (tablica 4.).

Budući da su centroidi dobiveni drugačije, a ne klasičnim klasteriranjem *mutnih* C-sredina (21 – 23), ovaj pristup čuva fleksibilnost funkcije *mutnog* pripadanja, a ipak klasificira opažanja u odgovarajuće stupnjeve CVM-a.

standing of what 'tall' is), while (190cm) is an exact measure of height. Using the CVM classification example mentioned earlier in the text, an instance could be 40% class II , 30% class III, and 30% class IV, which is a very common decision making concept in everyday life.

This is clearly illustrated in Figure 4 which shows fuzzy membership functions for two instances from the data set. Instance 1 clearly belongs to the first cluster (CVM-I class). Instance 2 belongs to the second cluster, although it could be reassigned into first and third cluster. An expert could easily classify this instance in the first or third cluster, using additional information from the specific case (e.g. patient's chronological age).

Using the fuzzy membership for CVM classification is almost natural, considering that the human growth is also a continuous process, where the growth states overlap.

Classification using modified fuzzy approaches

During the experiments, one problem was identified. The instances tend to group slightly differently in multidimensional space than the predicted CVM classes. In order to maintain the classes predicted by the literature, it is attempted to force the instances to group into five classes that more strictly correspond to CVM classes, using a modified Fuzzy C-means approach. The centroids of the classes were defined *a-priori*, using two approaches:

- The instances were classified into 5 classes using each of the 6 parameters separately, and then the class centroids were formed by aggregation. As a result, a centroid vector given in Table III was acquired.
- Centroid was made, based on the 50% of all orthodontists' measurements (shown in Table IV).

Considering that centroids were obtained in a different manner from that in the classical Fuzzy C-means clustering (21-23), this approach is named the 'modified' fuzzy approach. This approach preserves the flexibility of the fuzzy membership functions, and still classifies instances into adequate CVM classes.

Tablica 3. Centroidni vektori stupnja prema modificiranom klasteriranju *mutnih* C-sredina
Table 3 Class centroid vectors according to modified Fuzzy C-means clustering

MFC Class	C3conc	C4conc	C3par	C3bar	C4par	C4bar
Class-1	0.1016	0.0145	1.4435	1.9608	1.3613	2.1334
Class-2	0.7374	0.3819	1.2713	1.5993	1.1935	1.8240
Class-3	1.1312	0.7452	1.1576	1.3897	1.1106	1.6045
Class-4	1.6276	1.1875	1.0717	1.1674	1.0274	1.3629
Class-5	2.1572	1.9185	0.9633	0.9508	0.9352	1.0836

Tablica 4. Centroidni vektori stupnja prema mjerenjima specijalista
Table 4 Class centroid vectors according to the expert measurements

Em Class	C3conc	C4conc	C3par	C3bar	C4par	C4bar
Class-1	0.2255	0.0951	1.2067	1.8023	1.1613	1.8236
Class-2	0.9852	0.2205	1.1647	1.5993	1.1032	1.6386
Class-3	1.2780	0.5782	1.1136	1.3537	1.1151	1.4404
Class-4	1.5669	1.0188	1.0780	1.1609	1.0722	1.2126
Class-5	1.8955	1.2803	1.0609	1.0430	1.0645	1.1264

Rezultati

U prvom pokušaju tablica 1. korištena je kao referencija za centroidne vektore stupnjeva CVM-a. Za svaki slučaj za stupnjeve su izračunati *X(i)*, p-norme (za p=1 udaljenost d_1 je dobivena, za p=2 udaljenost d_2 je dobivena i za p=∞ dobivena je udaljenost d∞) i softver je preporučio stupanj CVM-a od kojega ima najmanju udaljenost, tj. od odgovarajućeg centroidnog vektora pojedinog stupnja. Prema tome su izračunati COIN-0 i COIN-1. Rezultati specijalista su u tablici 5.

Nakon postavljanja rasponskog vektora ***t*** na optimalnu vrijednost, rezultati su se malo poboljšali (malo iznad 3%). Rezultati metode klasteriranja K-sredina prikazani su u prvom redu tablice 6. Rezultati algoritma klasteriranja *mutnih* C-sredina u drugom su redu tablice 6.

Kad su centroidi oformljeni uz pomoć modificiranog *mutnog* pristupa, povećale su se sve mjere učinkovitosti (tablica 6., treći red). Kad su se rabili centroidni vektori kao u tablici 4., rezultati su se također poboljšali, kao što se i očekivalo (tablica 4., zadnji red).

Results

At the initiation of the study, Table I was used as reference for centroid vectors or 'normals' of CVM classes. For every instance *X(i)*, p-norms (for p=1 distance d_1 is obtained, for p=2 distance d_2 is obtained, and for p=∞ distance d∞ is obtained) resulting in the computer's program calculated classes. Consequently, the software suggested the CVM class the feature vector of which had the minimum deviation from the corresponding centroid vector of the class. Accordingly, COIN-0 and COIN-1 were calculated, indicating to which 'norm' or 'standard' [really, what centroid vectors] that particular individual resembled most closely. The results of these determinations are shown in Table V.

After setting the weighting (range) vector *t* to an optimal value, the results are slightly improved (about 3% improvement).

The results of the K-means clustering algorithm are presented in the first row of Table VI.

The results of the Fuzzy C-means clustering algorithm are presented in the second row of Table VI.

With the centroids formed by a modified fuzzy approach, all performance measures were increased (Table VI, row 3). When using the centroid vectors as in Table IV the results also improved, as expected (Table VI, last row).

Tablica 5. Eksperimentalni rezultati nakon korištenja različitih mjera udaljenosti i centroidnih vektora iz tablice 1.
Table 5 Experimental results using different distance measures and centroid vectors from Table I

Distance	COIN-0	COIN-1
Manhattan	57.35	94.79
Euclidean	55.93	92.89
Maximum	55.92	91.94

Tablica 6. Eksperimentalni rezultati za različite metode i centroidne vektore
Table 6 Experimental results for different methods and centroid vectors

Method	Centroid	COIN-0	COIN-1	COIN-F
K-means	K- means	54.03	97.63	
Fuzzy C-means	Fuzzy C.	55.92	98.10	78.19
Fuzzy C-means	Mod. Fuzzy C	63.04	99.53	78.67
Fuzzy C-means	Expert	70.62	99.06	77.25

Rasprava

Kad se primijeni najjednostavnija tehnika (centroidi i udaljenosti), može se vidjeti da je manhattanska udaljenost (norma L1) malo bolja od ostalih udaljenosti i da su stupnjevi dosta dobro predviđeni, posebice ako se analiziraju uz pomoć COIN-a 1.

Iz tablica 2. i 6. jasno je da centroidi K-sredina sadržavaju strukturu stupnjeva CVM-a (poboljšani COIN-1). Zanimljivo je da centroidi ne opisuju potpuno fizičke stupnjeve (CVM). To se uočava u tablici 2. u kojoj se može vidjeti da, primjerice, element C3-conc centroidnog vektora nije monoton kroz taj stupanj.

Korištenjem klasifikacije K-sredina otkrivena je važna činjenica – iako se stupnjevi razlikuju prema geometrijskim parametrima, razvoj svakoga nije uvijek konstantan. To znači da se neke geometrijske karakteristike u pojedinim slučajevi-

Discussion

When using the simplest technique (centroids and distances), it can be seen that the Manhattan distance (L1 norm) slightly outperforms all other distances, and the classes are reasonably predicted, especially when analyzing COIN-1.

It is clear from Table II and Table VI that K-means centroids capture the overall structure of CVM classes (improved COIN-1). Interestingly, the centroids do not fully interpret the physical meaning of the classes (CVM). This is clearly illustrated in Table II where it can be seen that, e.g. element C3conc of the centroid vector is not monotonous throughout the classes.

Using K-means classification, an important fact was discovered. Although the classes are distinct by their geometrical parameters, the development of each one of them is not always consistent. This means that certain geometrical charma razvijaju prije drugih, što procjenu klasifikacije CVM-a čini teškom. Kako bi se ilustrirala ta činjenica, na slici 5. je prikazana raspodjela prema stupnjevima samo za parametre trećeg kralješka (u smanjenom 3D prostoru) korištenjem deklariranog stupnja specijalista. Očito je da se ti stupnjevi preklapaju i da stroga klasifikacija nije najbolji način za rješavanje problema.

Centroidi *mutnih* C-sredina, kada se izračunaju, pokazuju istu anomaliju kao C3-conc u slučaju korištenja K-sredina. Premda korištenjem *mutnog* pristupa rezultati COIN-0 i COIN-1 nisu znatno poboljšani (tablica 6.), nakon analize parametra COIN-F jasno je da 78,2 posto procjena specijalista ima vjerojatnost od barem 30 posto. Granica od 30 posto odabrana je radi statističke značajnosti za izabrani stupanj. Treba istaknuti da, ako su svi od 5 stupnjeva jednako vjerojatni, funkcija pripadnosti bila bi 20 posto.

To znači da, premda se procjena specijalista i algoritma razlikuje vjerojatno samo u jednom stupnju (COIN-1 je oko 98%), mišljenje specijalista je numerički opravdano 80 posto. Ta pogreška učinjena na kraju s procjenom stupnja CVM-a nije tako značajna jer numerički parametri upućuju na to da je procjena više nego vjerojatna.

Zaključak

Iz rezultata se uočava da je potpuno automatizirana klasifikacija slučajeva u stupnjeve CVM-a težak problem jer: ne razvijaju se svi parametri linearno kroz stupnjeve, zato što svaki pacijent ima svoj trend rasta; ortodonti se koriste dodatnim podacima za procjenu stupnja CVM-a (poput kronološke dobi), kako bi ih mogli kombinirati s geometrijskim karakteristikama; zato što su mjerenja obavljena poluautomatski, moguće su pogreške – tome u prilog govori to što je u svim pokusima relativno nizak COIN-0 bio bolji ako bi se rabila potpuno automatizirana segmentacija slika i označavanje pojedinih obilježja; centroidni vektori trebali bi se transformirati u površine određenih stupnjeva, što bi omogućilo bolju procjenu stupnjeva; trebalo bi imati više pacijenata i više specijalista za procjenu i mjerenje svojstava; trenutačno se CVM-metoda ne može preporučiti kao jedini klinički kriterij za određivanje ortodontske terapije.

Ovo svojstvo ostaje kao smjernica za budući rad. Klasična (standardna) metoda CVM-a oslanja se na sposobnost kliničara da odredi stupanj maturacije kralježaka. Klasifikacija *mutne* pripadnosti ima velik potencijal i može pomoći stručnjacima u procjeni stupnja CVM-a i zato bi se trebala razvijati. Naša aplikacija omogućuje stručnjacima da ocijene grafikon sličan slici 4. u realnom vremenu (tijekom analize radiograma) i može biti velika pomoć u procjeni određivanja stupnja CVM-a, posebice ako stručnjaci nisu sigurni u njegovu točnost.

acteristics in some cases develop earlier than the other, and that makes the CVM class difficult to assess. To illustrate this fact, Figure 5 shows the distribution of the classes for just the 3rd vertebrae parameters (in reduced 3-d space), using the expert declared CVM classes. It is obvious that adjacent classes overlap each other, and that strict classification is not the best way to make the growth prediction.

The fuzzy C-means centroids, when calculated, show the same anomaly in C3conc, as the K-means do. Although by using all Fuzzy approaches the results of COIN-0 and COIN-1 were not greatly (Table VI), analyzing separately the parameter COIN-F makes it clear that 78.2% of the expert guesses result in the probability of at least 30% . The 30% threshold is chosen because it gives statistical significance to the chosen class. Note that if all the 5 classes were equally likely to occur, the membership functions would be essentially equal, or about 20% per class.

This means that, although the experts' and the algorithm's results differ, likely by not more than one class (COIN-1 is around 98%), the expert opinion numerically coincided with about 80% subjects. The error that was possibly made with the assessment of the CVM class is not clinically significant, because numerical parameters obtained by the developed software indicate that the assessments were somewhat optimistic or early.

Conclusions

It is suggested that the fully automatic classification of the CVM classes is a difficult problem. Following factors contribute to the ambiguities: not all parameters develop linearly throughout the classes, because all patients have their own developmental pattern; orthodontists use additional information to assess the CVM stage (such as chronological age); this information should be combined with the geometrical characteristics of the cervical vertebrae; the measurements are made semi-automatically, so they are error-prone, implying that relatively low COIN-0 in all experiments could be better if the fully automatic image segmentation and feature detection were used; the class centroid vectors should be transformed to class areas instead, which would enable better assessment of the classes; more patients and a larger group of 'experts' [orthodontists and anthropologists] should evaluate and measure these features; currently the CVM method cannot be recommended as a strict and definitive clinical guideline for the timing of orthodontic treatment.

The presented features provide useful guidelines for future studies. Classic (or standard) CVM method relies on the clinician's ability to determine the stage of maturation of the vertebrae. The Fuzzy membership classification shows a significant potential in assisting clinicians in CVM class assessment and thus it should be further studied. Our application enables the experts to review graphs similar to those in Figure 4 in real time (e.g. during the radiographic image analysis), that can be of valuable assistance in the process of CVM assessment, especially when the clinicians are unsure of the actual CVM class.

Abstract

Introduction: Effectiveness of different numerical techniques for use in semi-automatic assessment of cervical vertebral maturation stages (CVM) using radiograph images was investigated. **Methods:** Lateral cephalographs of 211 patients were recorded and stored in a digital form. Using the specially developed software application, orthodontic experts marked and measured several characteristic cephalometric parameters for every patient. The results of these measurements were used to automatically determine the cervical vertebral maturation stage using numerical techniques, including the K-means clustering and the Fuzzy C-means clustering. These results were compared with the assessment made manually by the trained orthodontists.**Results:** The best results were achieved using the modified Fuzzy-C means clustering. Identification of the correct CVM stage was around 70%, while the assessment including the adjacent classes [+/- 1 developmental stage] was over 99%. **Conclusions:** Experimental results show that it may be possible to develop a fully automated system to assess CVM stages, although there are still minor issues that need to be addressed before the method's implementation in the clinical practice.

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