



INSTITUT ZA ONKOLOGIJU
I RADIOLOGIJU SRBIJE

UNIVERZITET U BEOGRADU

MEDICINSKI
FAKULTET



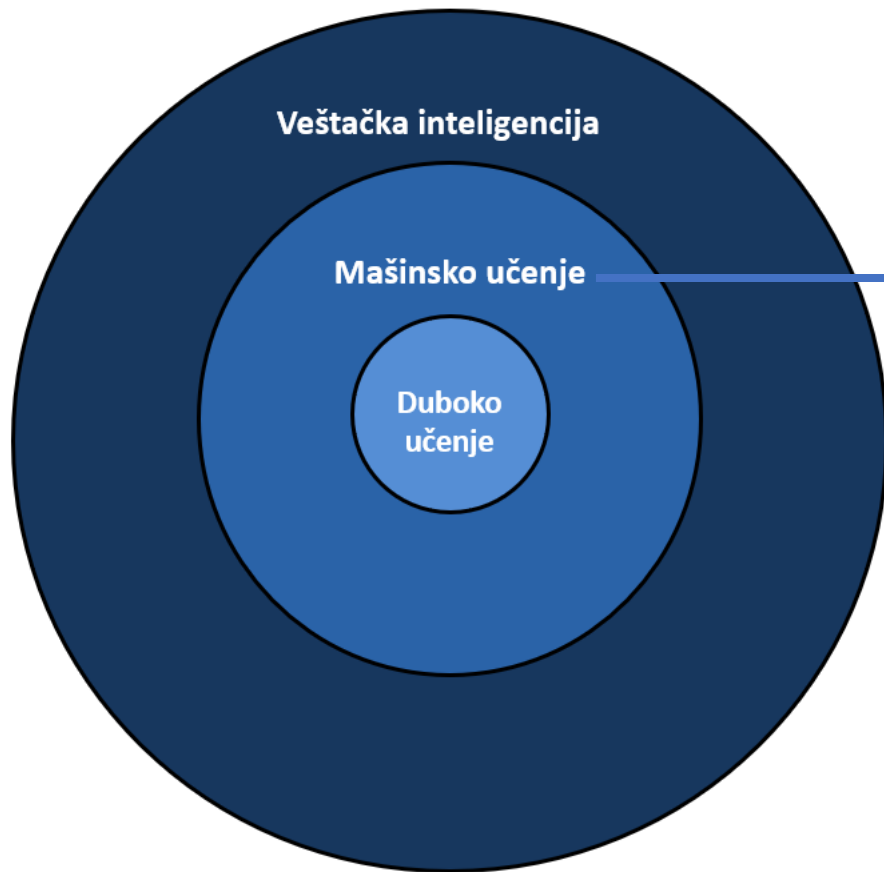
Osnove nadgledanog mašinskog učenja i njihova praktična primena u nuklearnoj endokrinologiji

**Marina Popović Krneta
Dragana Šobić Šaranović**

Pregled predavanja:

- Mašinsko učenje
- Trenutni izazovi u nuklearnoj endokrinologiji
- Razvoj modela mašinskog učenja na primeru iz nuklearne endokrinologije

„Skup različitih računarskih tehnika koje omogućavaju kompjuterskim sistemima da donose zaključke bez potrebe za direktnim programiranjem“- Arthur Lee Samuel



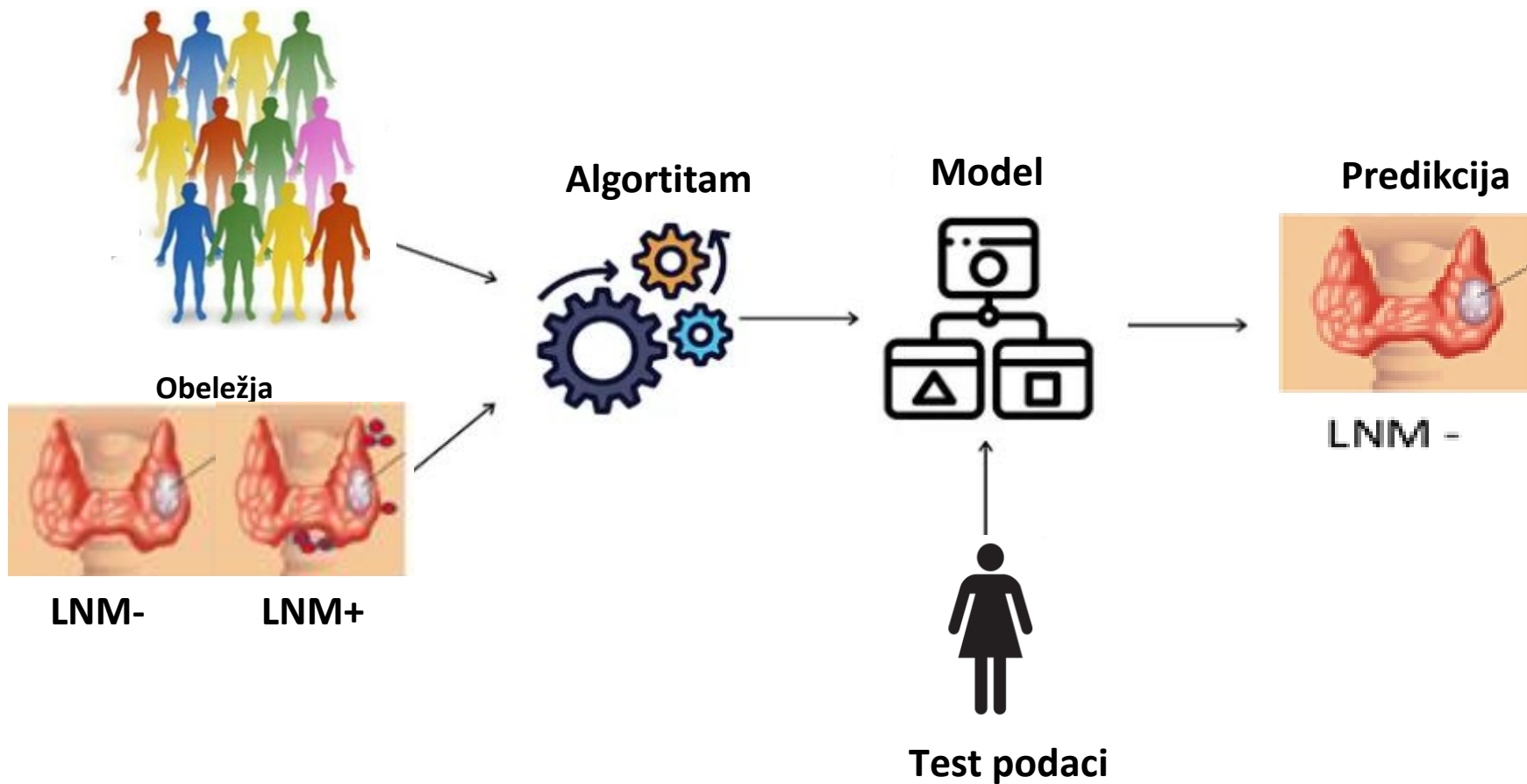
- Nadgledano mašinsko učenje (engl. *Supervised Learning*)
- Nenadgledano mašinsko učenje (engl. *Unsupervised Learning*)
- Učenje uz podsticaje (engl. *Reinforcement Learning*)

Article

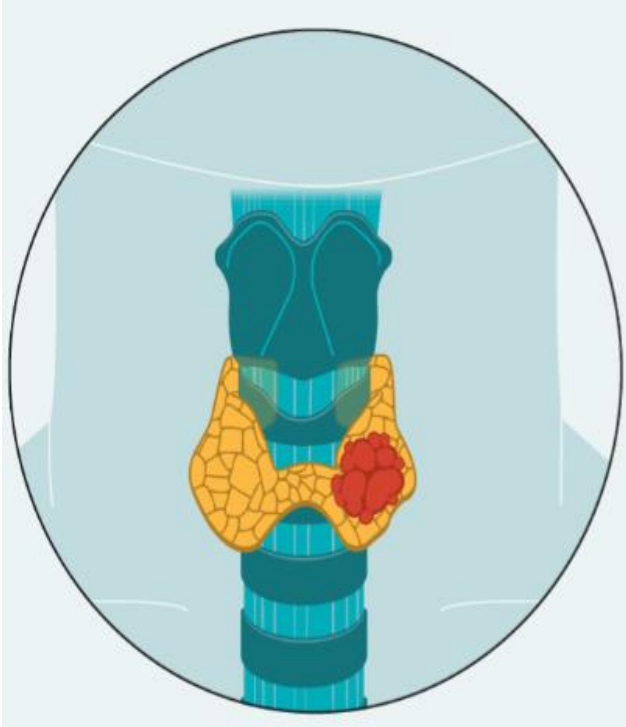
Prediction of Cervical Lymph Node Metastasis in Clinically Node-Negative T1 and T2 Papillary Thyroid Carcinoma Using Supervised Machine Learning Approach

Marina Popović Krneta ^{1,*}, Dragana Šobić Šaranović ^{2,3}, Ljiljana Mijatović Teodorović ^{1,4}, Nemanja Krajčinović ⁵, Nataša Avramović ⁵, Živko Bojović ⁵, Zoran Bukumirić ⁶, Ivan Marković ^{2,7}, Saša Rajšić ⁸, Biljana Bazić Džorović ¹, Vera Artiko ^{2,3}, Mihajlo Karličić ⁹ and Miljana Tanić ^{10,11,*}

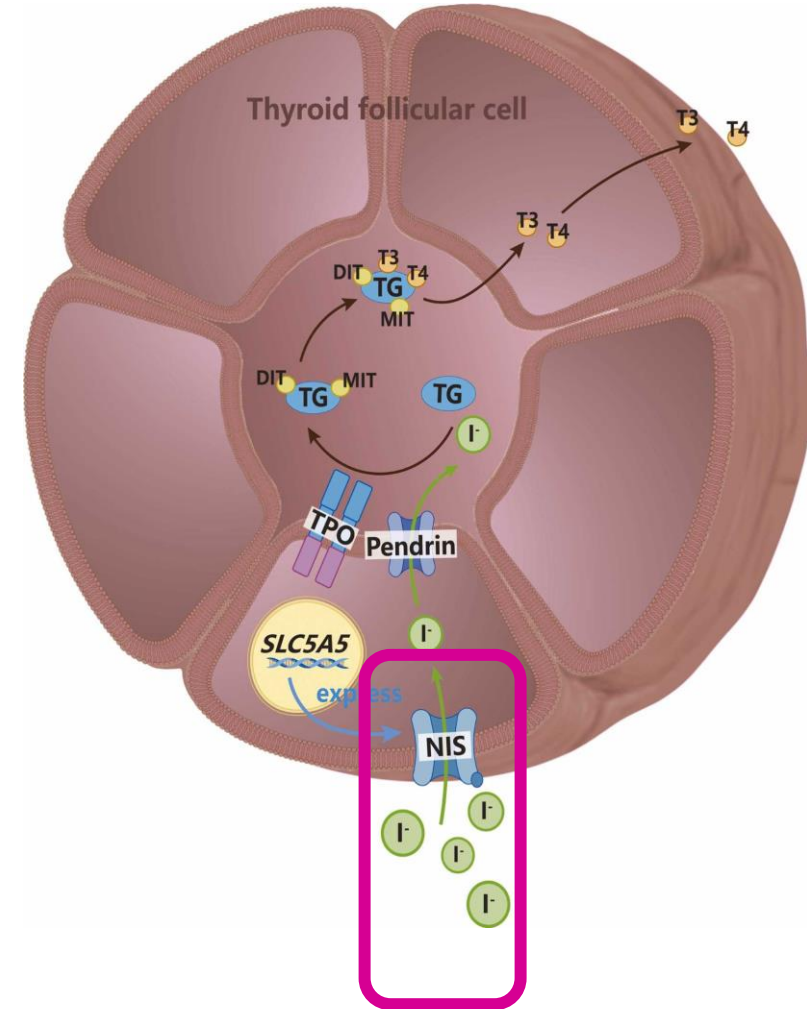
Pacijenti sa tiroidnim karcinomom



NUKLEARNA ENDOKRINOLOGIJA/ONKOLOGIJA



Yetman, D. Healthline, 2022.



Shen H., Drug Resist Updat. 2024

- Diferentovani karcinomi štitaste žlezde (tiroidee)
- Potreba za radiojodnom terapijom i određivanje doze radioaktivnog joda

One-size-fits-all approach



Radiojodna terapija (RAJ):

- *Nije indicovana kod svih hirurški operisanih pacijenata*
- *Odluka o primeni RAJ terapije donosi se **na osnovu postoperativno procenjenog rizika od recidiva***

- Totalna tiroidektomija
- Terapija radioaktivnim jodom
- Hormon-supresivna terapija

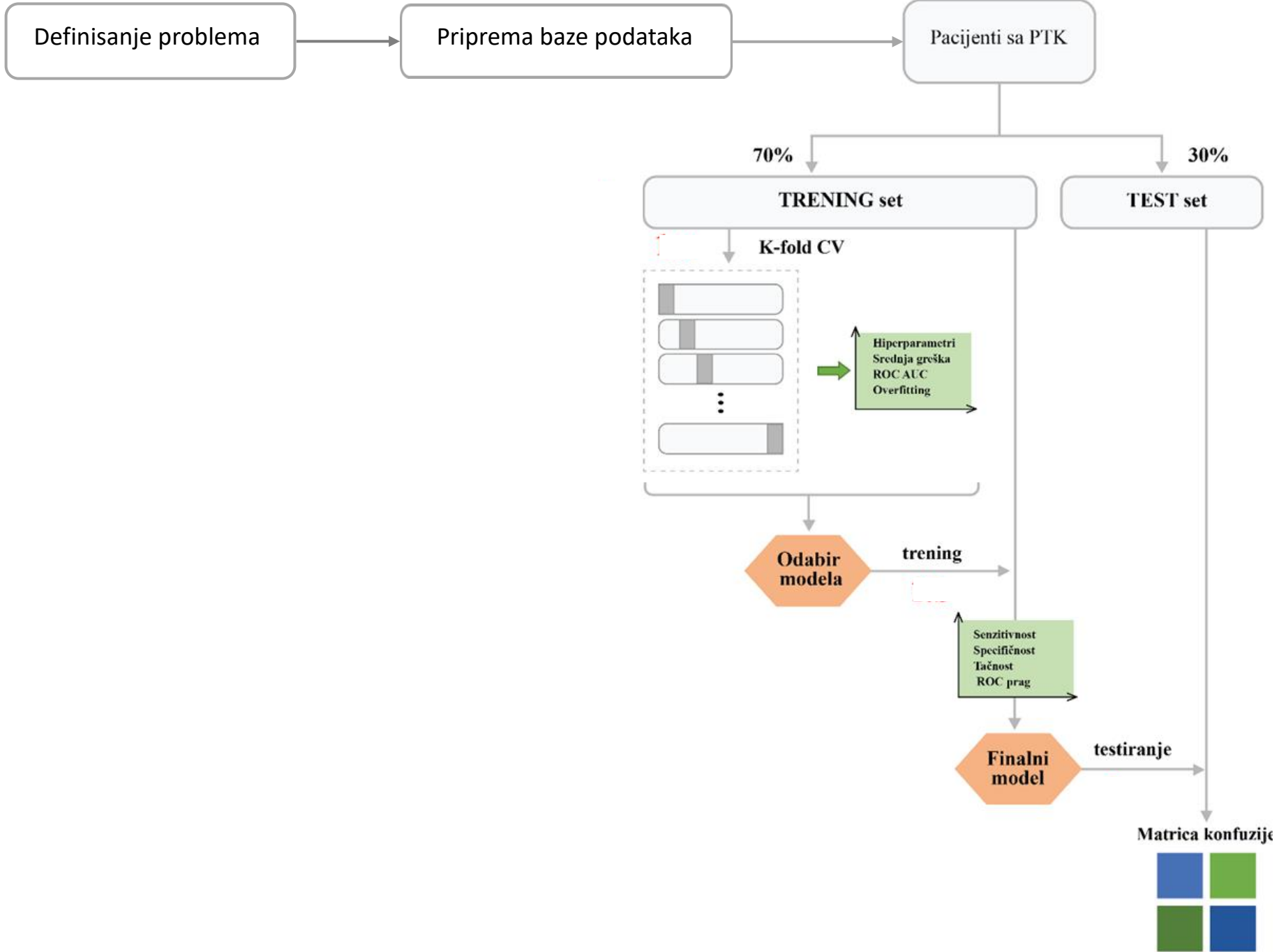
Klinička potreba:

- **Trenutno ne postoji adekvatan, jasno definisan sistem za procenu postoperativnog rizika od recidiva**
- Postojeće smernice su brojne i često neusaglašene
- Postojeće smernice se oslanjaju isključivo na patohistološke faktore rizika bez uključivanja specifičnih bioloških i molekularnih markera

Cilj:

Razviti model **nadgledanog mašinskog učenja** koji vrši predikciju odgovora na radiojodnu terapiju i koji se može koristiti kao sistem podrške pri donošenju odluke o dozi radiojodne terapije. Naglasak pri razvoju modela bio je na postizanju što manjeg broja **lažno negativnih** rezultata.

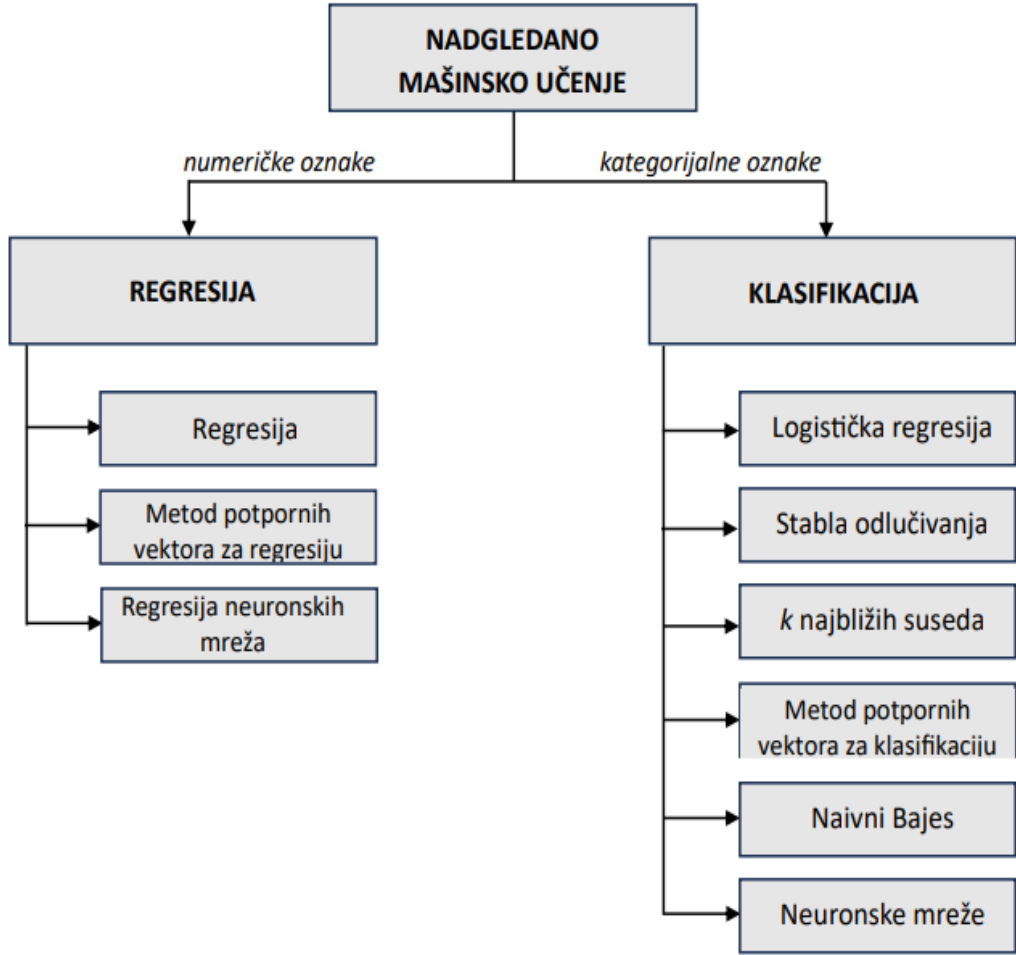
Identifikovati prediktivne faktore neadekvatnog terapijskog odgovora.



Definisanje problema:

Odgovor na RAJ terapiju:

1. Odličan
2. Neadekvatan



Badillo i sar., Clin Pharmacol Ther., 2020

* Odgovor na terapiju procenjivan je najmanje 9 meseci nakon sprovedene radiojodne terapije na osnovu validiranog, dinamičkog sistema stratifikacije rizika

Nadgledano mašinsko učenje:

➤ **Algoritam K-najbližih suseda (engl. *k-Nearest Neighbor- K-NN*)**

Metrike rastojanja : Euclidean, Manhattan, Chebyshev, Minkowski, Hamming, Canberra, Bray–Curtis, Jaccard, Matching, Dice, CityBlock, Rogers–Tanimoto, Russell–Rao, Sokal–Michener, and Sokal–Sneath,

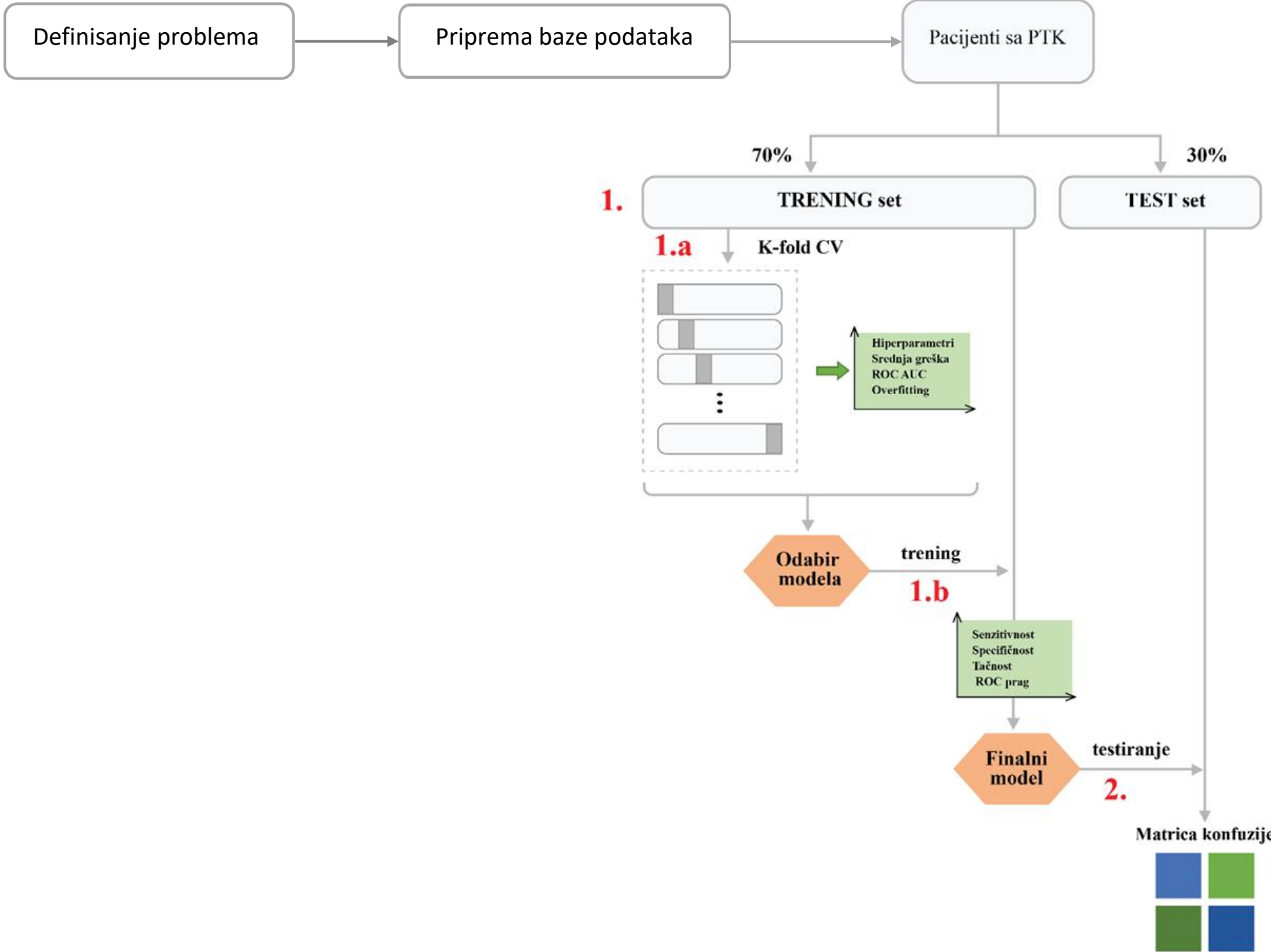
➤ **Metod potpornih vektora (engl. *Support Vector Machines - SVM*)**

Kerneli: polynomial, radial basis function (RBF), sigmoid,

➤ **Stablo odluke (engl. *Decision Tree - DT*),**

➤ **Logistička regresija (LR)**

Solveri: Liblinear, the Limited-memory Broyden–Fletcher–Goldfarb–Shanno(L-BFGS), Newton-conjugate gradient method (Newton-CG).

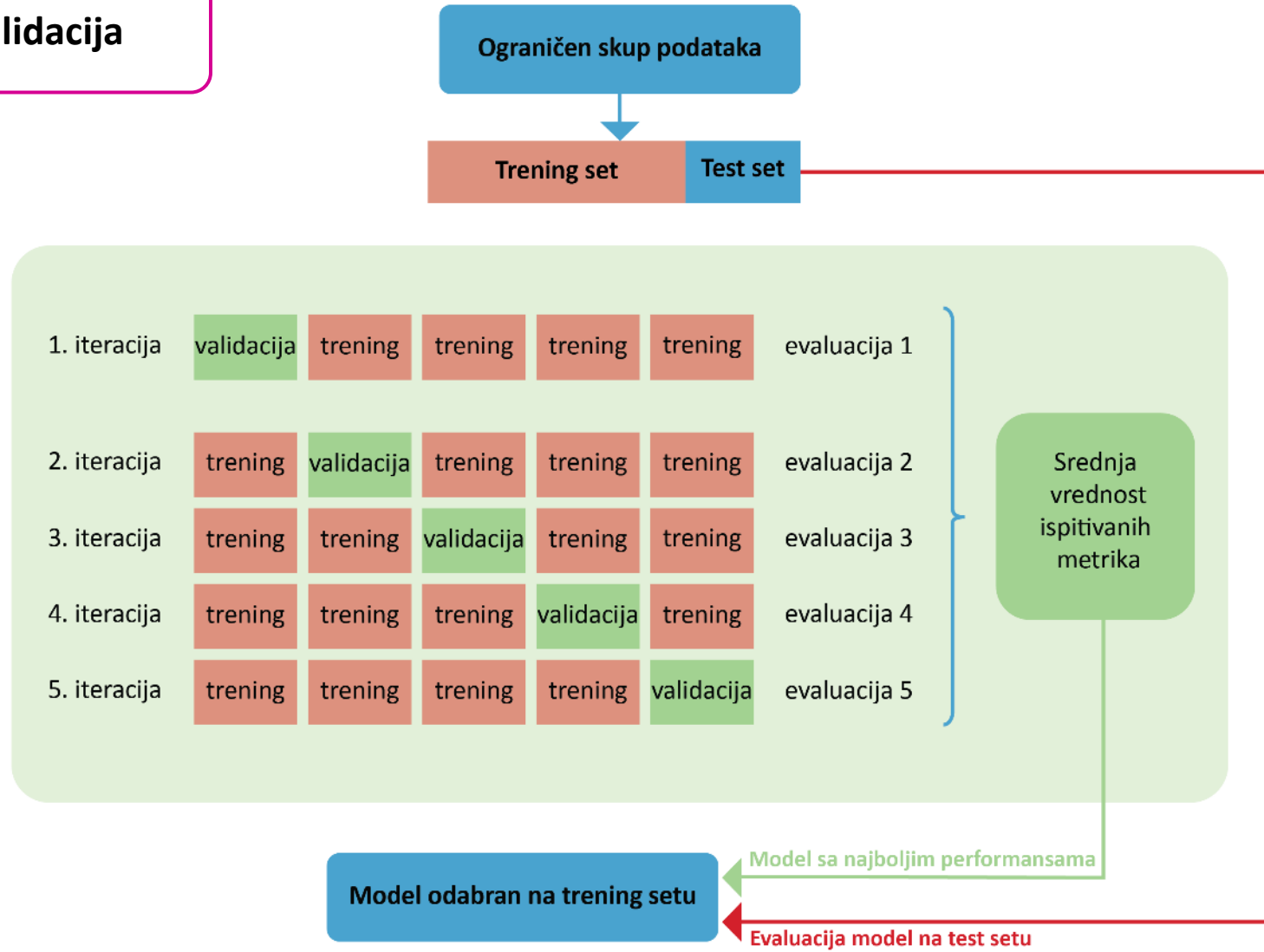


double dipping !!!

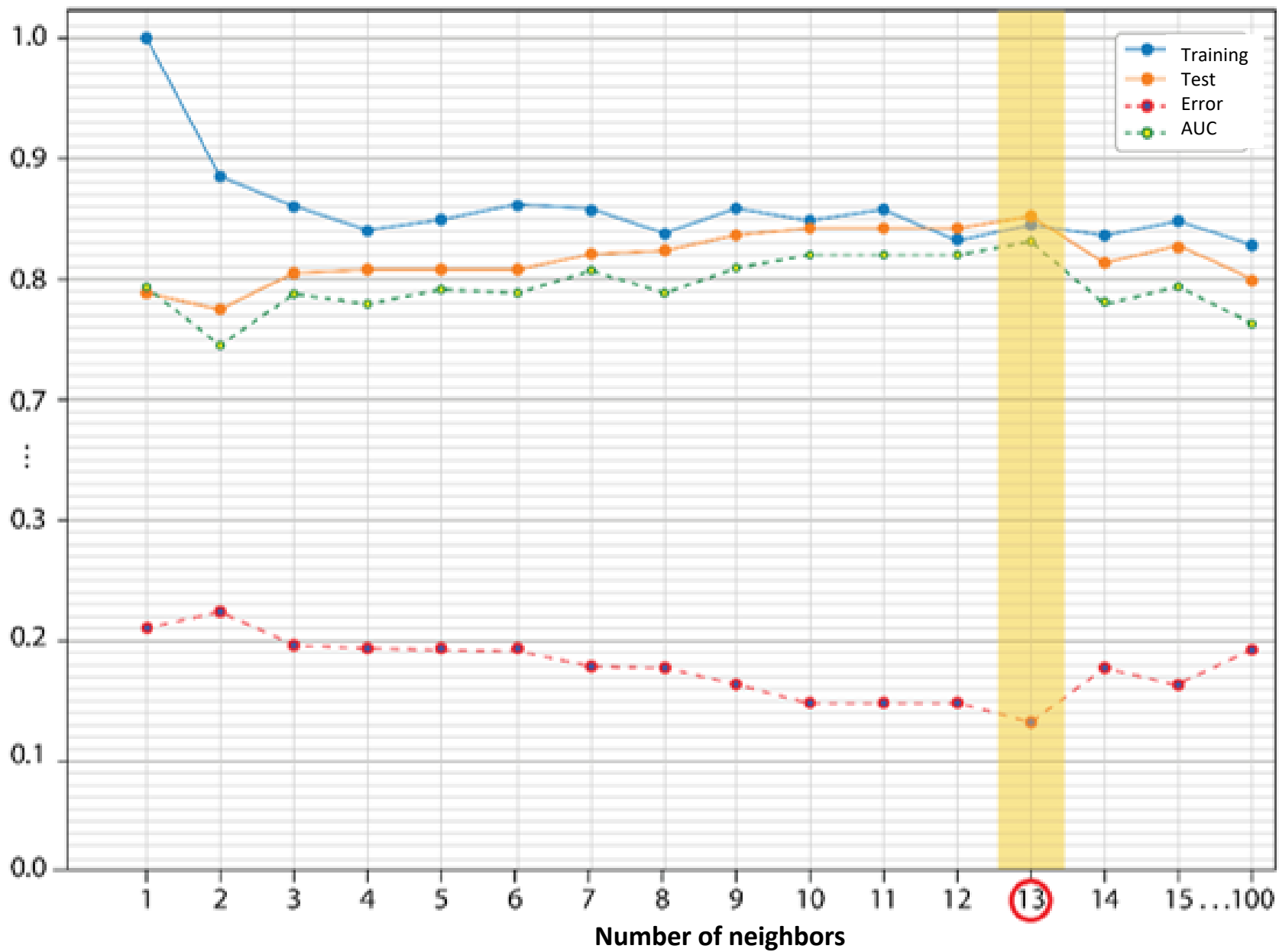
Karakteristike	Odličan (n = 39)	Noadekvatan (n =28)	p-value
<i>Veličina tumora (mm), medijana (opseg)</i>	10.0 (4-50)	17.0 (5-60)	0.011
<i>Broj tumorskih fokusa, n (%)</i>			
1	28 (71.8)	12 (42.9)	
2	9 (23.1)	3 (10.7)	0.002
≥ 3	2 (5.1)	13 (46.4)	
<i>Bilateralnost, n (%)</i>			
ne	33 (84.6)	16 (57.1)	
da	6 (15.4)	12 (42.9)	0.012
<i>Ekstratiroidna ekstenzija (ETE), n (%)</i>			
ne	28 (71.8)	12 (42.8)	
mikroskopska ETE	8 (20.5)	8 (28.6)	
ekstenzivna ETE	3 (7.7)	8 (28.6)	0.029
<i>Limfonodalne metastaze (LNM), n (%)</i>			
ne	9 (23.1)	0 (0.0)	
da	30 (76.9)	28 (100)	0,008
<i>Broj limfnih nodusa, medijana (opseg)</i>	4 (1-12)	5.5 (1-28)	0,014
<i>Odnos limfnih nodusa, medijana (opseg)</i>	0.17 (0.01-0.70)	0.46 (0-1)	<0,001
<i>MI, n (%)</i>			
ne	39 (100)	24 (85.7)	0.027
da	0 (0.0)	4 (14.3)	
<i>Preablativni TG (ng/ml), medijana (opseg)</i>	1.2 (0.1-10.3)	40.73 (0.04-428)	<0,001

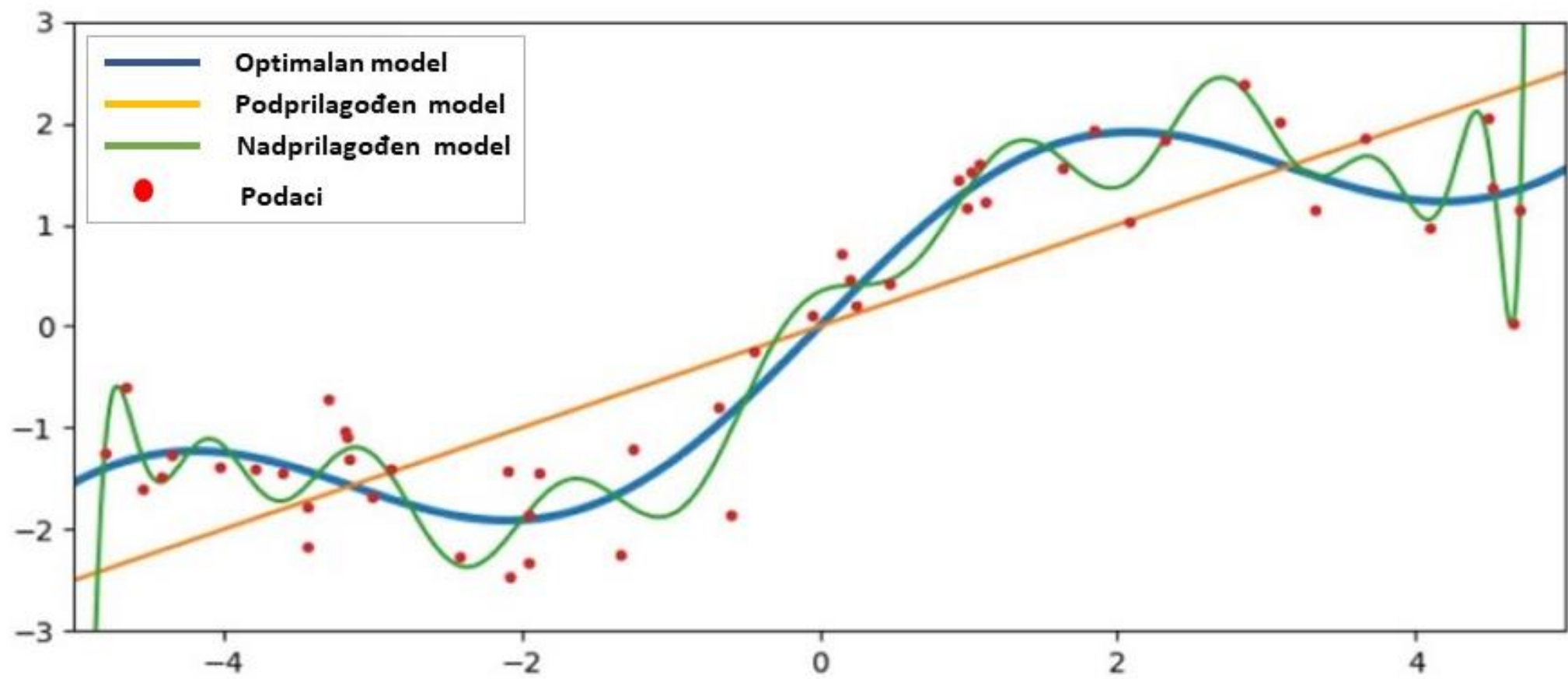
+ Godine, Pol, Histopatološki tip tumora, *BRAF* V600 E mutacija

5-ostruka unakrsna validacija



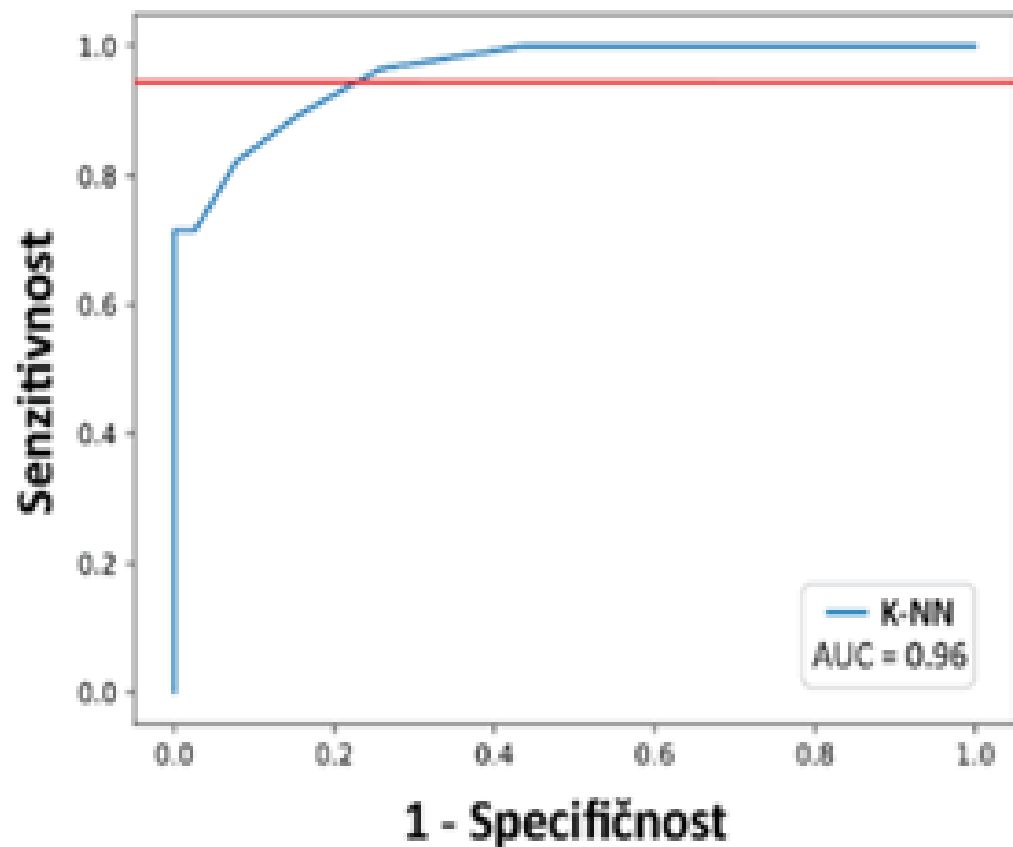
K-NN model
Canberra





SVM model, RBF kernel





	Prag	Senzitivnost	Specifičnost
0	100.0000%	0.0000%	100.0000%
1	92.3077%	3.5714%	100.0000%
2	84.6154%	35.7143%	100.0000%
3	69.2308%	39.2857%	100.0000%
4	61.5385%	53.5714%	100.0000%
5	53.8462%	64.2857%	100.0000%
6	46.1538%	71.4286%	100.0000%
7	38.4615%	71.4286%	97.4359%
8	30.7692%	82.1429%	92.3077%
9	23.0769%	89.2857%	84.6154%
10	15.3846%	96.4286%	74.3590%
11	7.6923%	100.0000%	56.4103%
12	0.0000%	100.0000%	35.8974%

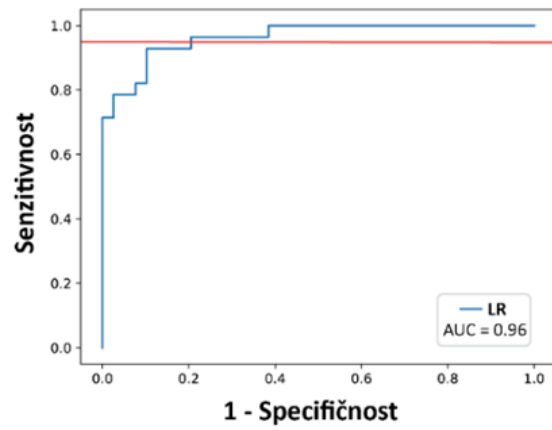
Smanjenje broja lažno negativnih rezultata=povećanje senzitivnosti (senzitivnost iznad 95%)

		Ishod koji je predvideo ML model		
		1	0	
Stvarni ishod	1	Stvarno pozitivni (TP)	Lažno negativni (FN)	Senzitivnost = $\frac{TP}{TP + FN}$
	0	Lažno pozitivni (FP)	Stvarno negativni (TN)	Specifičnost = $\frac{TN}{TN + FP}$ FPR = $\frac{FP}{FP + TN}$
		PPV $\frac{TP}{TP + FP}$	NPV $\frac{FN}{TN + FN}$	Tačnost $\frac{TP + TN}{TP + TN + FP + FN}$

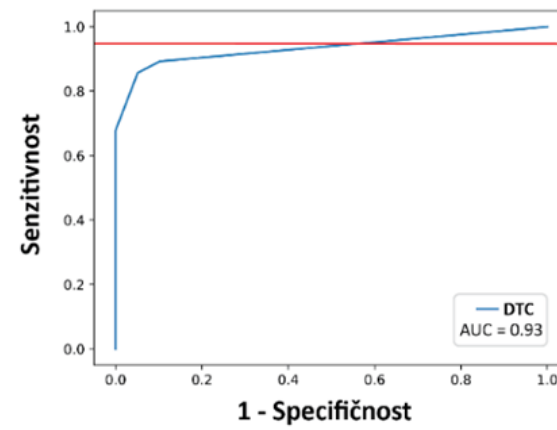
$$F1 = \frac{2 * PPV * Senzitivnost}{PPV + Senzitivnost}$$

$$F2 = \frac{5 * PPV * Senzitivnost}{4 * PPV + Senzitivnost}$$

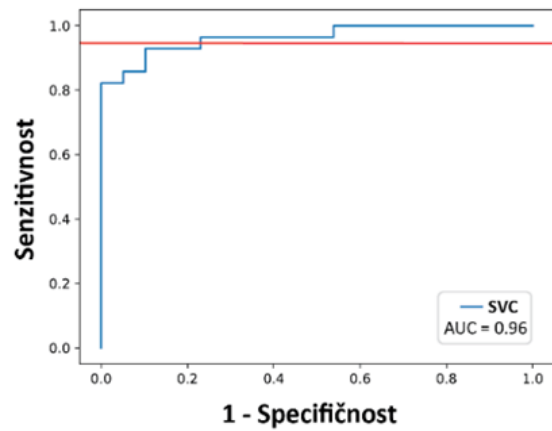
A



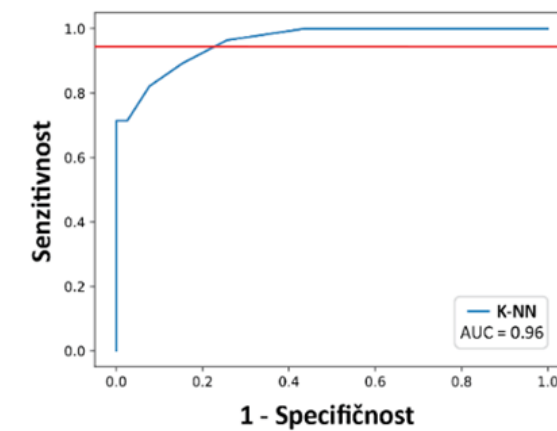
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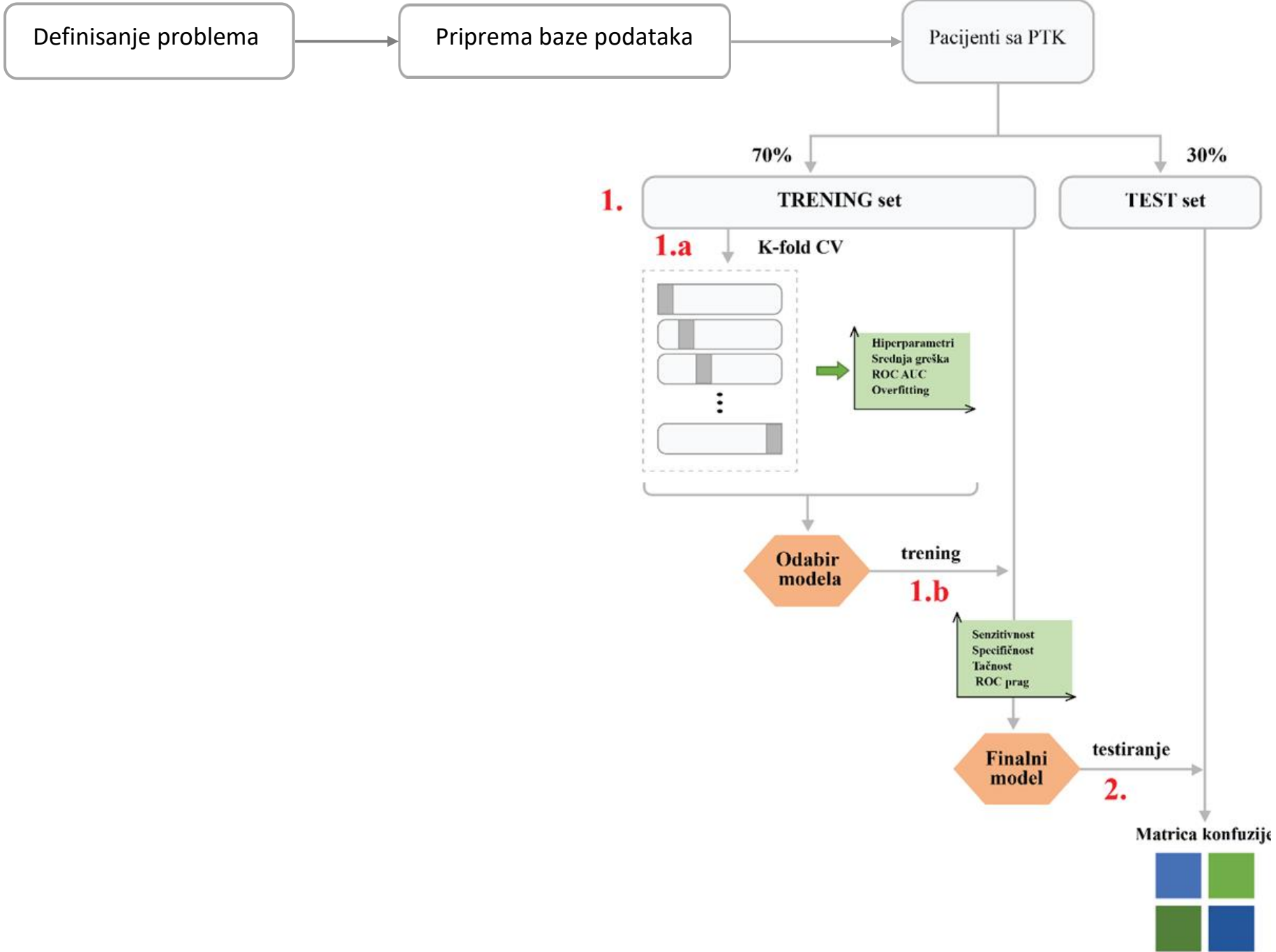
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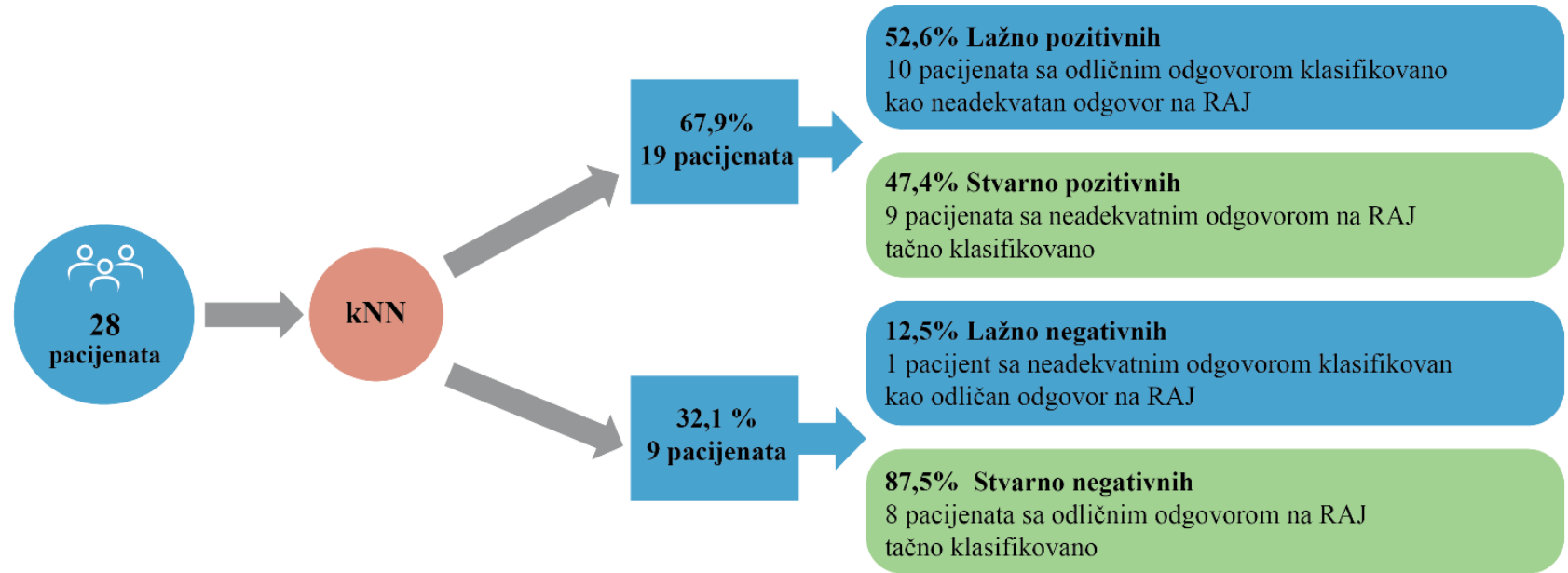
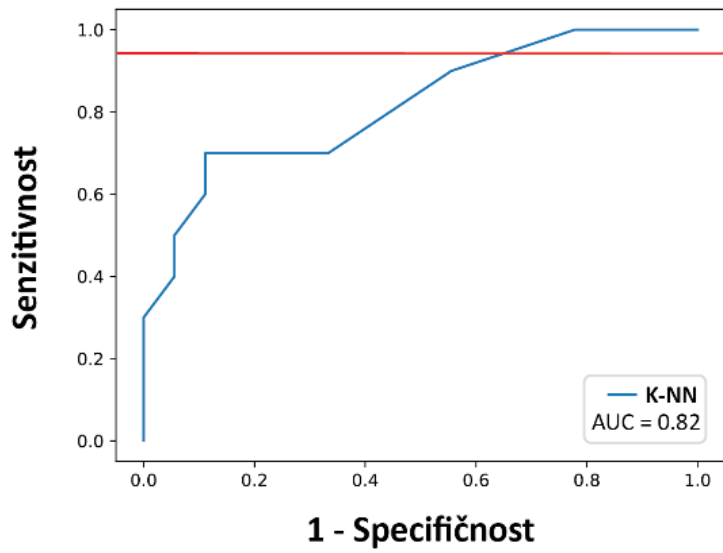


D



ML model	Senzitivnost	Specifičnost	NPV	PPV	Tačnost	F1	F2
KNN	0,96	0,74	0,96	0,71	0,82	0,82	0,90
SVM	0,96	0,58	0,96	0,60	0,73	0,74	0,86
LR	0,96	0,64	0,96	0,64	0,77	0,77	0,87
DT	0,95	0,35	0,91	0,49	0,59	0,65	0,80





ML model	Senzitivnost	Specifičnost	NPV	PPV	Tačnost	F1	F2
kNN	0,90	0,44	0,89	0,47	0,61	0,62	0,76



Postoperative thyroglobulin as a yard-stick for radioiodine therapy: decision tree analysis in a European multicenter series of 1317 patients with differentiated thyroid cancer

Luca Giovanella^{1,2} · Lisa Milan¹ · Wolfgang Roll³ · Manuel Weber⁴ · Simone Schenke⁵ · Michael Kreissl⁵ · Alexis Vrachimis⁶ · Kim Pabst⁴ · Tuncel Murat⁷ · Petra Petranovic Ovcaricek⁸ · Burkhard Riemann³ · Luca Ceriani¹ · Alfredo Campenni⁹ · Rainer Görge⁴

Table 6 Predictive values, accuracy, and overall performance of decision tree model and prevalence of positive post-treatment whole-body scintigraphy, respectively, in different centers and the overall population

Decision tree model	Center 1 (n=208)	Center 2 (n=208)	Center 3 (n=83)	Center 4 (n=371)	Center 5 (n=447)	All (n=1317)
PPV	66.7%	49.9%	18.1%	59.98%	86.6%	67%
NPV	87.6%	95.9%	95.9%	86.46%	87.34%	89.9%
Accuracy	84.6%	93.3%	85.6%	87.88%	87.27%	87.8%
AUC	0.708	0.699	0.642	0.610	0.708	0.680
Positive PT-WBS (%)	20.2%	6.7%	6%	13.2%	20.1%	15.2%

> J Thorac Oncol. 2015 Apr;10(4):629-37. doi: 10.1097/JTO.0000000000000447.

Validation of a multiprotein plasma classifier to identify benign lung nodules

Anil Vachani ¹, Harvey I Pass, William N Rom, David E Midthun, Eric S Edell, Michel Laviolette, Xiao-Jun Li, Pui-Yee Fong, Stephen W Hunsucker, Clive Hayward, Peter J Mazzone, David K Madtes, York E Miller, Michael G Walker, Jing Shi, Paul Kearney, Kenneth C Fang, Pierre P Massion

Affiliations + expand

PMID: 25590604 PMID: PMC4382127 DOI: 10.1097/JTO.0000000000000447

Senzitivnost:92%

Specifičnost:20%

NPV 92%,

PPV 26%

Pacijenti sa solitarnim nodusima u plućima

Masena spektrometrija za analizu uzoraka plazme i identifikaciju plazma proteina koji omogućavaju lakšu diferencijaciju prirode promena u plućima

ClinicalTrials.gov; No.: [NCT01752114-PANOPTIC](https://clinicaltrials.gov/ct2/show/study/NCT01752114)
(LG3BP_Human, C163A_Human)

Skrining nodusa u plućima

Medicar/Medicaid- US



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Juan Liu,
Huazhong University of Science and
Technology, China

Reviewed by:

Hao Zhang,
Dalian Medical University, China
Changming An,
Chinese Academy of Medical

Application of Machine Learning Algorithms to Predict Central Lymph Node Metastasis in T1-T2, Non-invasive, and Clinically Node Negative Papillary Thyroid Carcinoma

Jiang Zhu^{1†}, Jinxin Zheng^{2†}, Longfei Li³, Rui Huang⁴, Haoyu Ren^{1,5}, Denghui Wang¹, Zhijun Dai^{2,4} and Xinliang Su^{1,4}

Senzitivnost 67%

Specifičnost 67%

Stopa lažno negativnih rezultata 34%

Article

Prediction of Cervical Lymph Node Metastasis in Clinically Node-Negative T1 and T2 Papillary Thyroid Carcinoma Using Supervised Machine Learning Approach

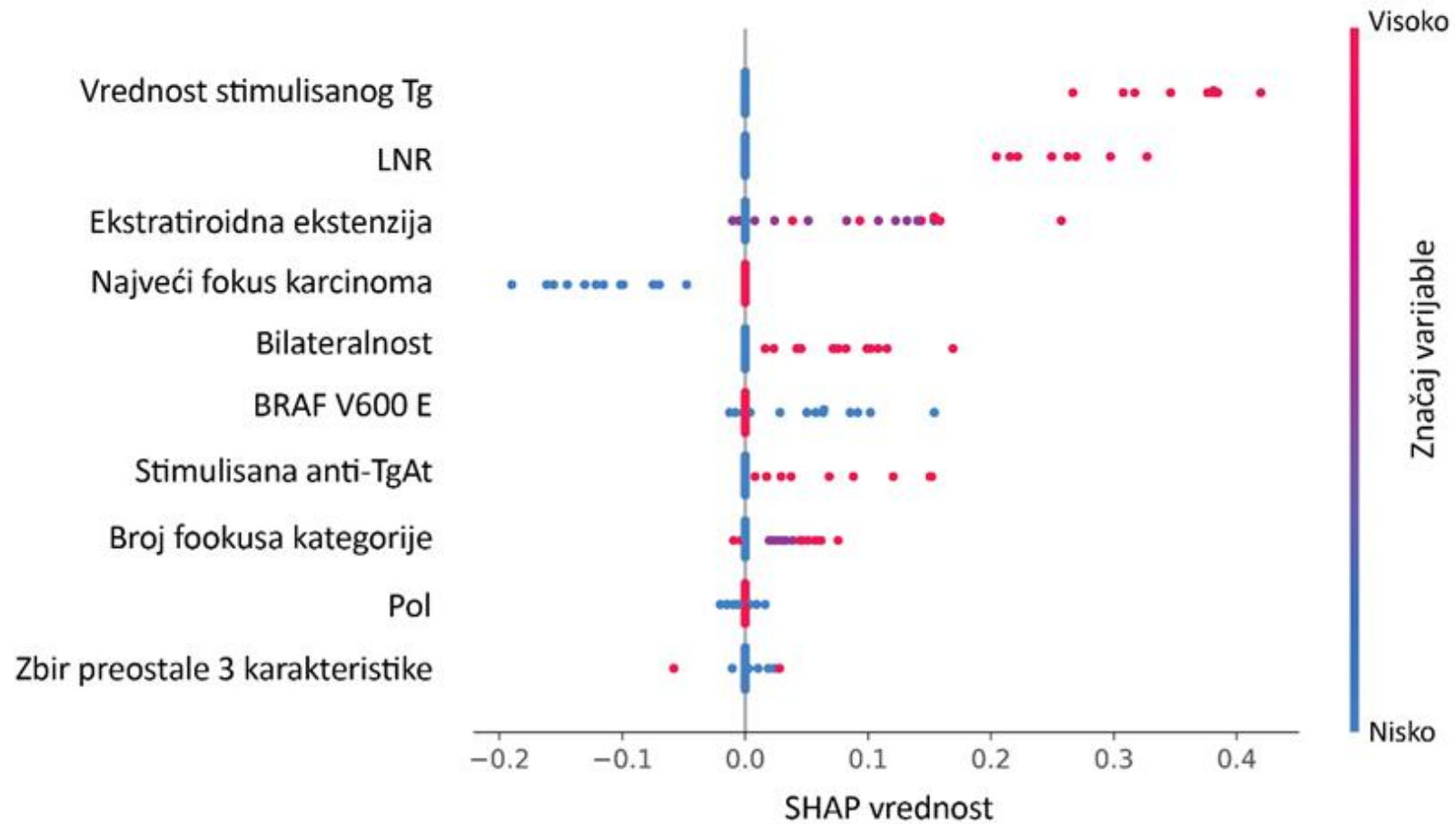
Marina Popović Krneta^{1,*}, Dragana Šobić Šaranović^{2,3}, Ljiljana Mijatović Teodorović^{1,4}, Nemanja Krajčinović⁵, Nataša Avramović⁵, Živko Bojović⁵, Zoran Bukumirić⁶, Ivan Marković^{2,7}, Saša Rajšić⁸, Biljana Bazić Džorović¹, Vera Artiko^{2,3}, Mihajlo Karličić⁹ and Miljana Tanić^{10,11,*}

Senzitivnost 98%

Specifičnost 27%

Stopa lažno negativnih rezultata 7%

Shapley Additive Explanations (SHAP) Analysis



Ni vrednost stimulisano Tg, ni LNR nisu deo standardnih sistema klasifikacije.



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