



# LÉČBA KARCINOMU NEZNÁMÉHO PRIMÁRNÍHO ZDROJE S METASTÁZAMI DO KRČNÍCH UZLIN

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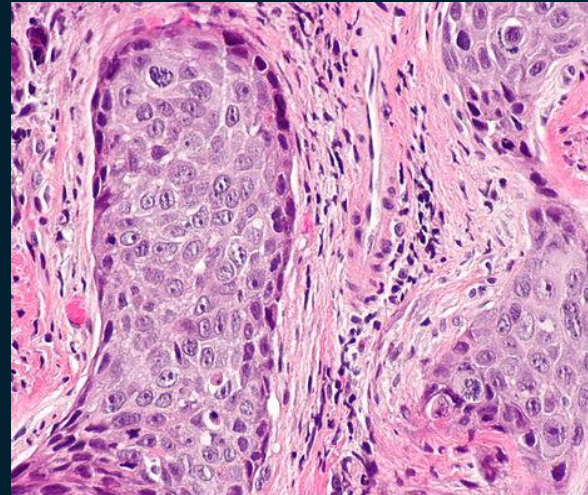
# Co to je ?

- Histologicky ověřené metastázy do krčních uzlin bez nálezu primárního nádoru

~ 5% nádorů hlavy a krku



>90% SCC



# Příčiny non-detekce primárního nádoru

**Teorie  
nevědomosti**

**Teorie  
neschopnosti**

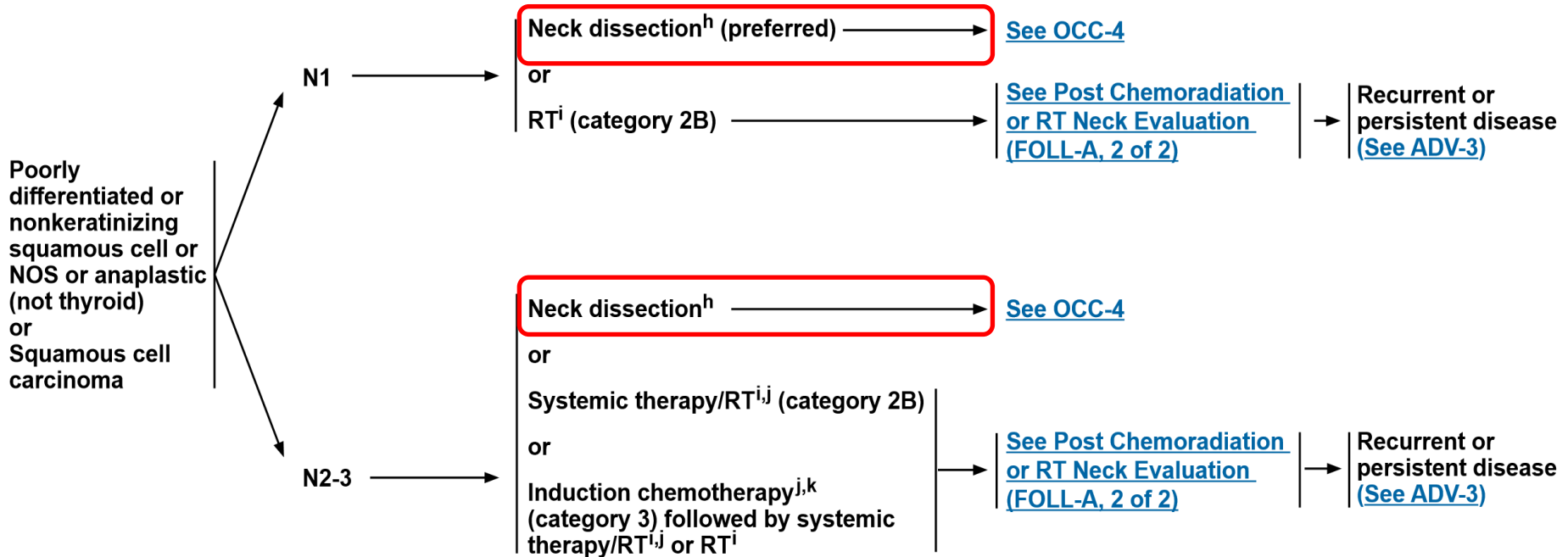
**Regionální  
léčba**

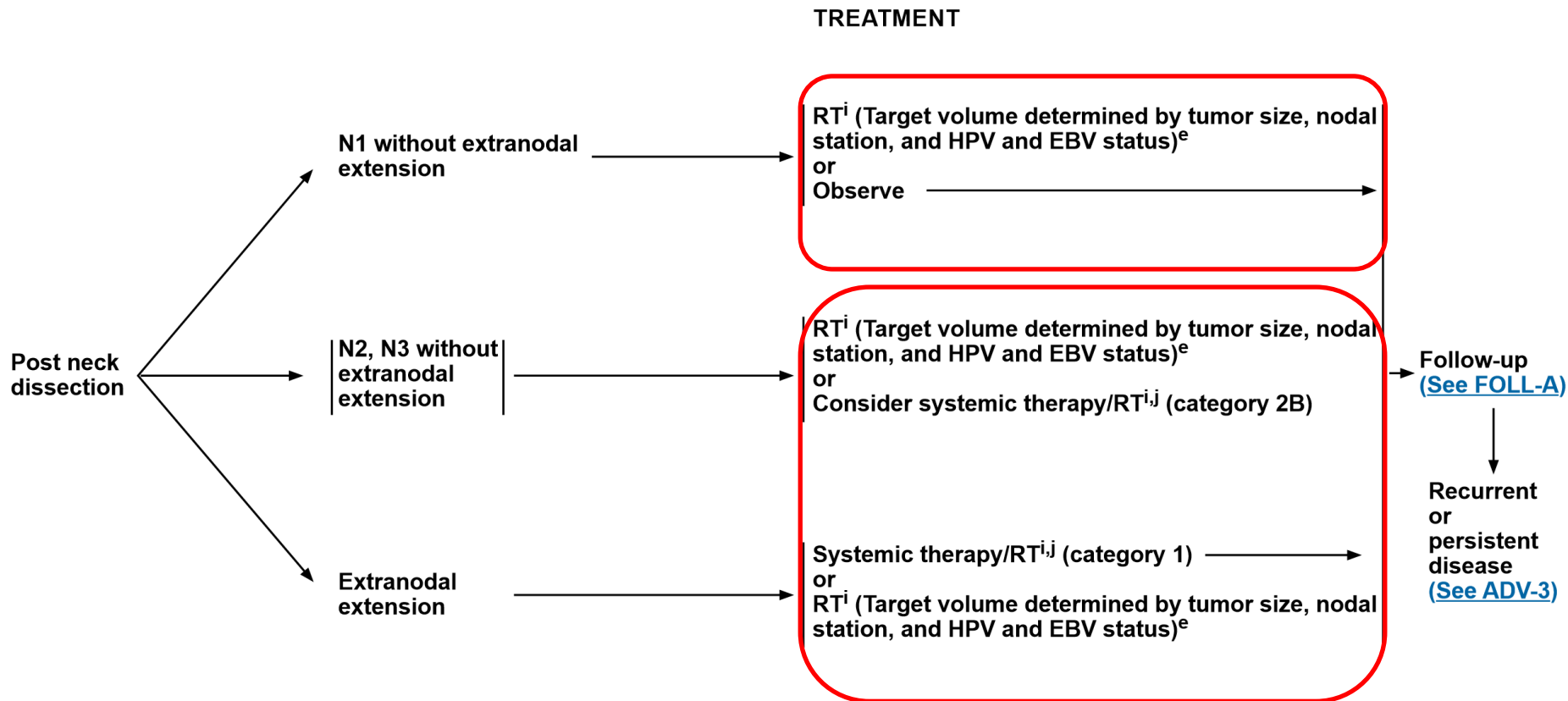
**Lokoregionální  
léčba**



### HISTOLOGY

### DEFINITIVE TREATMENT





# EBM

- Prospektivní klinická hodnocení

**NIC**

- Retrospektivní klinická hodnocení souborů s dostatečnou četností

**NIC**

- Jiná pro klinickou praxi upotřebitelná data

**NĚCO MÁLO**

# CHIR vs CHIR + RT ?

- Retro-, **n=277** (1975-1995)
  - 81% oboustranná RT, 10% jednostranná RT, 9% bez RT
  - **5y-LC 15% vs 54%** (p<0,0001)
- Retro-, **n=106** (1969-1994)
  - N1/N2a uni- vs multimedialita **RC 93% vs 67%** (p=0,14)
    - $\geq$ N2b **RC 74% vs 50%** (p=0,08)
  - Primární zdroj onemocnění
  - 5y-OS

**CHIR + RT > CHIR**

# CHIR + RT vs RT ?

- Retro-, **n=41** (1994-2001)
  - **4y-LRC** 76% vs 75% NS
  - **4y-OS** 85% vs 86% NS
- Retro-, **n=48** (1980-2000)
  - + Chirurgie HR 0.4 (p=0,042)
- Retro-, **n=45**
  - 5y-OS 63% NS

- Retro-, **n=52**
  - 5y-DSS 75% vs 73% NS
- Retro-, **n=52**
  - 5y-OS 68% vs 68% NS
  - 4y-LRC 75% vs 74% NS

**CHIR + RT > RT**

*Head Neck 2014*  
*Otolaryngol Head Neck Surg. 2008*  
*ong, Head Neck 2002*

*Reddy, IJROBP Neck 1997*  
*Aslani, Head Neck 2007*



# Ipsilat RT vs bilat RT + faryng osa ?

- Retro-, 5 center, **n=277** (1975-1995)
  - 81% bilat, 10% ipsilat, 9% ND
  - **5y-RC 27% vs 51%** (p=0,05)
  - 5y-DSS **28% vs 45%**
- Retro-, **n=60**
  - 18% bilat + faryng.osa, 40% bilat, 42% ipsilat
  - 5y-OS 67% vs 75% vs 55% NS
  - Prim.tu: faryngeální osa + bilat vs ipsilat/bilat **13% vs 23%**
- Retro-, **n=82**
  - 53% bilat + faryng.osa, 47% ipsilat
  - **bilat ↑ OS** (p=0,0003)

📖 *Grau, Radiother Oncol 2000*

📖 *Lu, Tumori 2009*

📖 *Boscolo-Rizzo, ORL 2006*

# Celá faryng osa (naz,oro,hyp,lar) ?

- Retro-, **n=17**, blok stínící larynx u AP pole
  - **LC** 100%, 5y-CSS 88%, 5y-OS 82%
- Retro-, **n=18**, IMRT, bilat + oro, nas
  - 2y-OS 74%, **2y-RC** 89%
- Retro-, **n=179**, ipsilat + bilat faryng osa
  - **LC** 100%

**RT bilat + faryng osa > RT ipsilat**

📖 *Mendenhall, Am J Otolaryngol 2001*

📖 *Wallace, American Journal of Otolaryngology 2011*

📖 *Lu, Oral Oncology 2009*

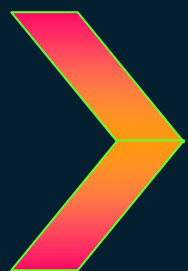
# RT vs RCHT

- Retro-, **n=140** (1999-2006)
  - RT 60-70 Gy (n=64) vs RT + CHT CDDP qw (n=76)
  - 5y-DFS 42% vs 54% NS
  - **5y-OS 22% vs 40%** (p<0,05)
- Retro-, **n=60**
  - 2y-PFS 79% vs 80% NS
  - 5y-OS 90% vs 90% NS

**RCHT u ECE+, pN2-3?**

*Chen, nt J Radiat Oncol Biol Phys 2011*  
*Chen, Indian J Med Paediatr Oncol 2009*

# Léčebný algoritmus



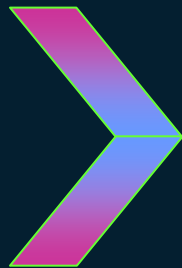
**CHIR → RT**

**ANO**  
nejspíše i u pN1



**RT bez CHIR**

**ANO**  
pokud nelze CHIR



**Extenzivní RT**

**ANO**  
faryngeální osa + krk bilat  
+/- larynx & hypofarynx



**CHRT**

**ANO**  
u ↑ rizika

# Metaanalýza

33 klinických studií (1973-2015)

## CHIR + RT vs RT

RR n=1582

**5y-OS 0,66**

95% CI 0,52–0,83, p = 0,0004

**5y-RC 0,74**

95% CI 0,59–0,92, p = 0,008

## Bilat RT vs Ipsilat RT

RR n=1449

**5y-DFS 0,81**

95% CI 0,64–1,03, p = 0,09

**5y-RC 0,61**

95% CI 0,41–0,91, p = 0,01

**5y-LC 0,44**

95% CI 0,26–0,77, p = 0,004

↑ **Akutní toxicita**

## RT krku vs RT krku + faryngeální osy

RR n=1347

**5y-DFS 0,75**

95% CI 0,61–0,92, p = 0,005

**5y-RC 0,72**

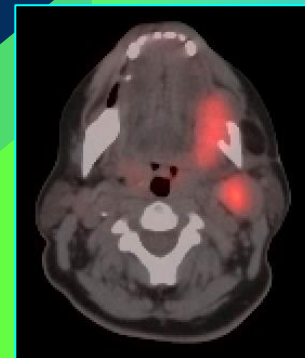
95% CI 0,56–0,92, p = 0,009

**5y-LC 0,23**

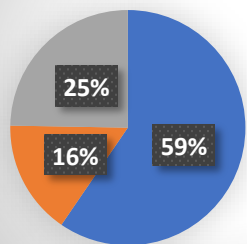
95% CI 0,12–0,45, p < 0,0001

# Soubor pacientů URO

- Retro-, **n=90** (2003-2017), medF/U žijících **86m**
- věk med 59 (31 – 82) , muži / ženy 65 / 25
- závažné komorbidity 67% (ACE $\geq$ 2 19%), duplex 9, triplex 1
- **PET / CT-PET 72%**

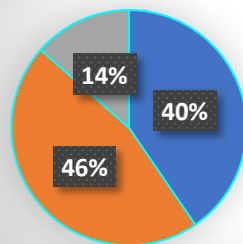


## Nikotinismus



- Chronický nikotinismus
- Exnikotinus >5y
- Nekuřák

## Etylismus

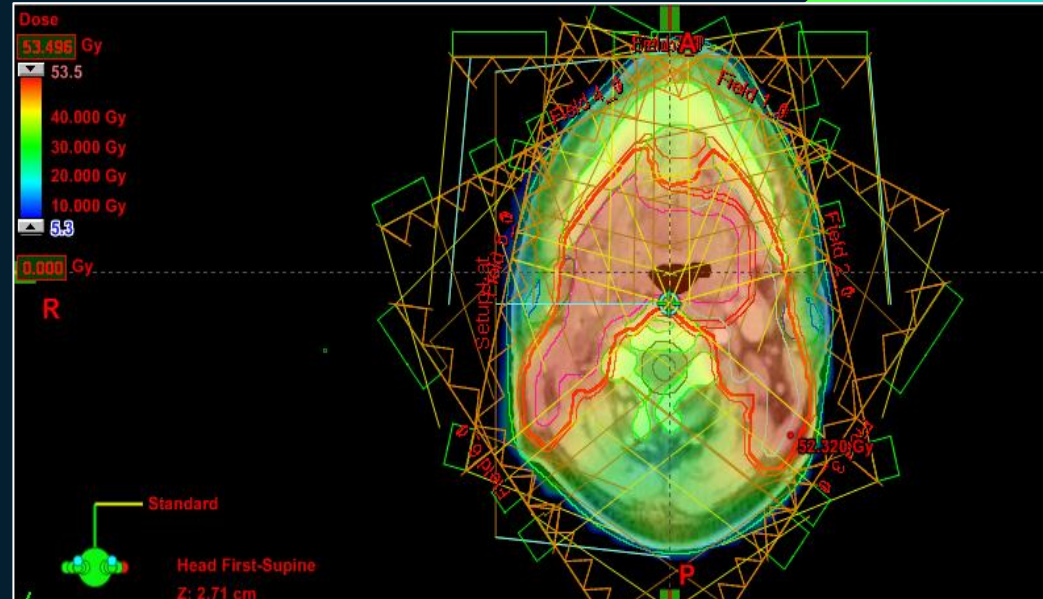
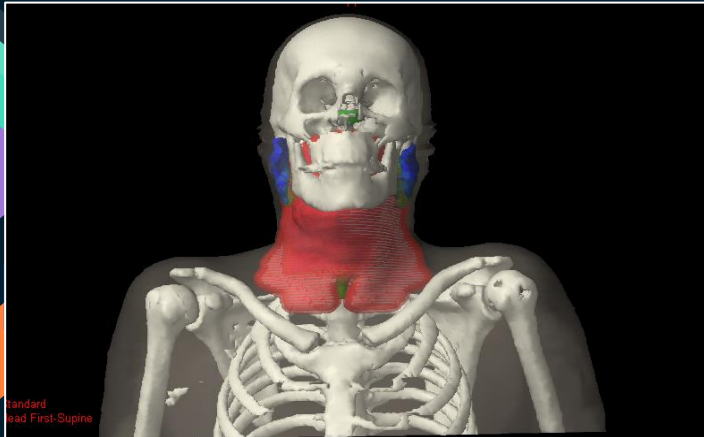
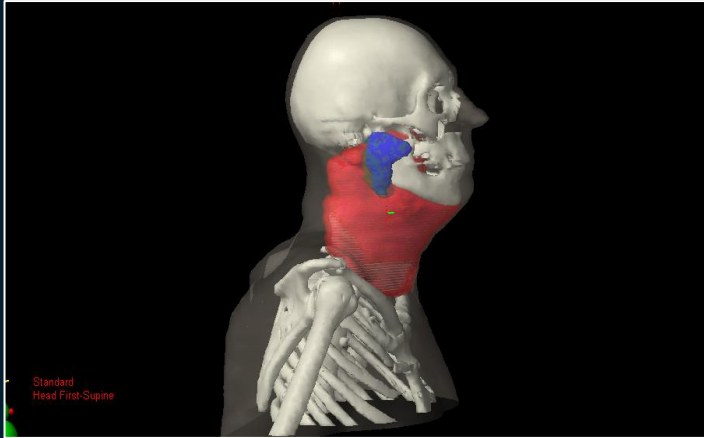


- Denně
- Příležitostně
- Abstinent

N-staging	n	%
<b>N1</b>	11	<b>12%</b>
<b>N2a</b>	19	<b>21%</b>
<b>N2b</b>	39	<b>43%</b>
<b>N2c</b>	9	<b>10%</b>
<b>N3</b>	12	<b>13%</b>

# Léčba

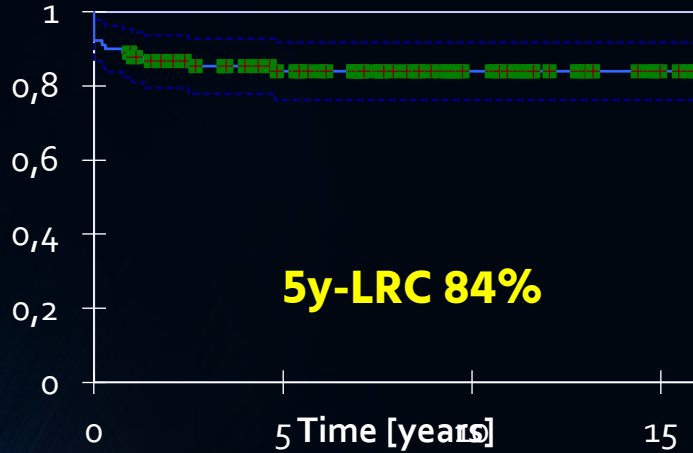
- CHIR ND **62%**; biopsie/ extirpace 38%
- RT (med 70Gy) **100%**  
osa + krk bilat 96%, IMRT 72%
- CHT (CDDP qw) **66%**
- HyT 14%



# Výsledky

## Lokoregionální kontrola

### LRC



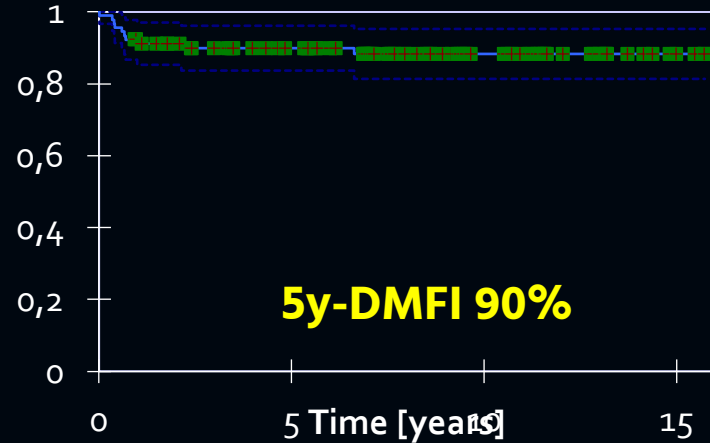
### Regionální selhání 12

- perzistence 7 (5 N3, 1 N2b, 1 N2c)
- regionální recidiva 5 (3-30m, ipsilaterálně ECE 100%, 4 N2b, 1 N2c)

Lokální selhání 2 (16,58m; dut.ústní 2)

## Distanční kontrola

### DFMI



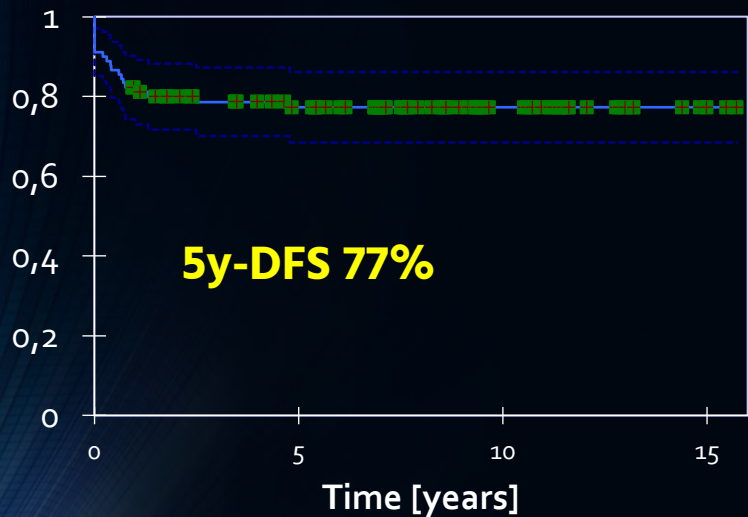
Distanční selhání 10 (1-80 m, 9 z toho <30m)

Plíce	4
Axilární uzliny	3
Játra	1
Multiorgánové	2

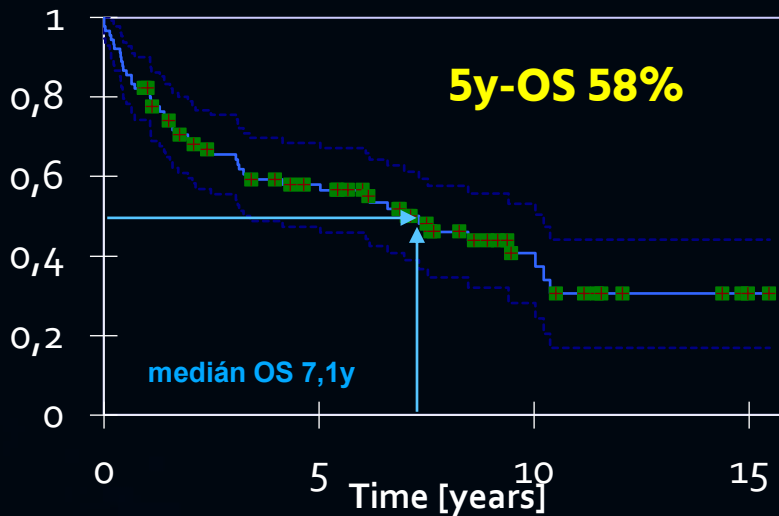


# Výsledky

*Přežití bez nemoci*  
DFS



*Celkové přežití*  
OS



48+

- progrese nádoru 15
- progrese duplicitního nádoru 6
- nenádorová mortalita 27

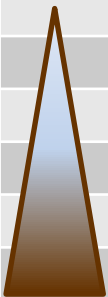
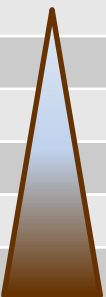
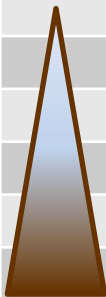
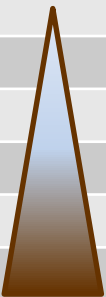
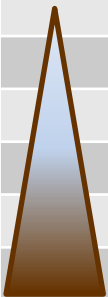
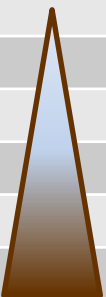
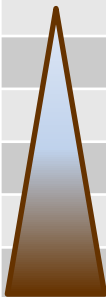
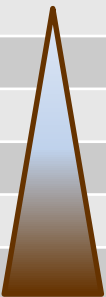
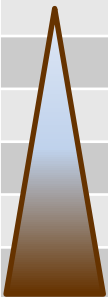
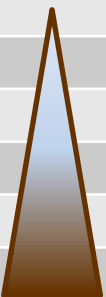
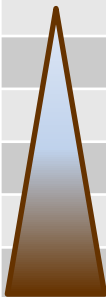
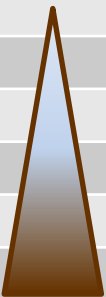
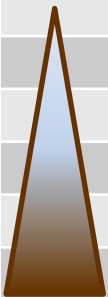
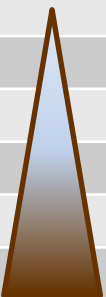
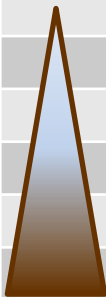
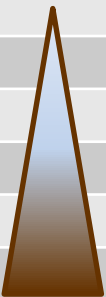
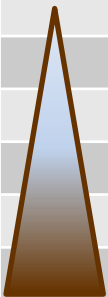
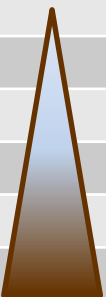
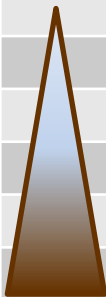
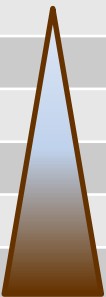
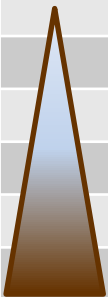
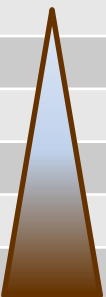
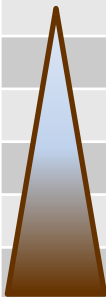
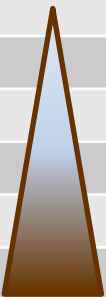

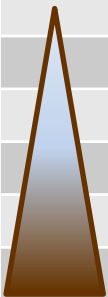
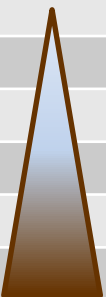
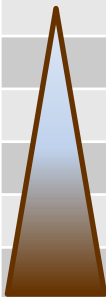
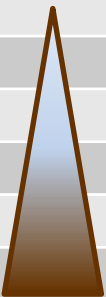
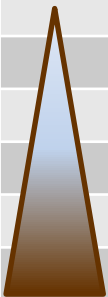
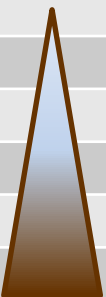
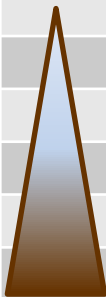
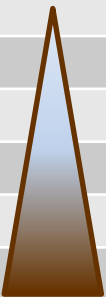
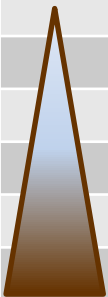
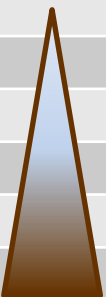
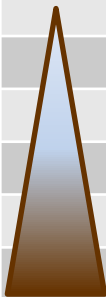
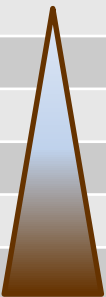
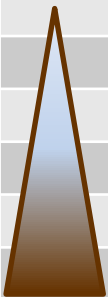
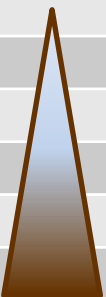
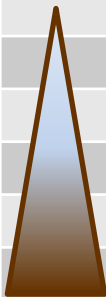
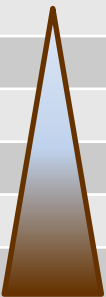
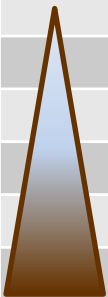
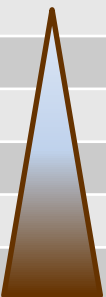
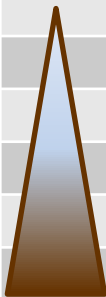
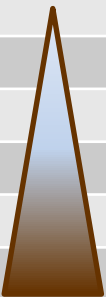

Gr.3/4 n=72	Sliznice	Kůže	Podkoží	Slinné žlázy	Oči	Uši	Hrtan	Mozek	Mícha
n	0	1	5	13	0	0	1	0	0
%	0%	1%	7%	18%	0%	0%	1%	0%	0%

n=72	Hypotyreóza	ORN
n	21	4
%	29%	6%

Hltan n=72	n	%
Gr.0	31	43%
Gr.1	29	40%
Gr.2	7	10%
Gr.3	2	3%
Gr.4	3	4%

**Pozdní  
toxicita**

**G3/4 35%**

autor	n	LC	RC	DM	OS
Harper 1990	69	88%	72%	-	48%
Glynne-Jones 1990	58	93%	64%	-	40%
Maulard 1992	113	90%	86%	84%	38%
Nguyen 1994	54	94%		80%	63%
Weir 1995	144	<b>79%</b> 93%	<b>51%</b> 51%	<b>80%</b> -	<b>25%</b> 41%
Sinnathamby 1997	63	 89%	 -	 -	 36%
Reddy 1997	52	 81%	 -	 -	 51%
Colletier 1998	136	 92%	 91%	 82%	 60%
Strojan 1998	56				 52%
Grau 2000	277	 -	 51%	 -	 36%
Iganej 2002	106	 82%	 72%	 91%	 53%
Tóthová 2006 	50	 -	 -	 -	 41%
Boscolo-Rizzo 2006	82	<b>96%</b> 88%	<b>98%</b>	<b>91%</b>	<b>89%</b> 25%
Frank 2007	52	<b>96%</b> 94%	<b>98%</b> 98%	<b>91%</b> -	<b>89%</b> 89%
Shukla 2009	140	 -		 84%	 40%
Rodel 2009	58		 67%		 41%
Lu 2009	60	 79%	 66%		 69%
Cuaron 2015	85	 -	 87%		
<b>Pála 2019 </b>	<b>90</b>	<b>96%</b>	<b>86%</b>	<b>91%</b>	<b>58%</b>

# Závěr

RT na oblast faryngeální osy & oboustranných krčních uzlin umožňuje trvalou kontrolu u většiny léčených pacientů

Časná toxicita vysoká, ale léčebně zvládnutelná, z pozdní toxicity dominuje zhoršení polykacích funkcí v důsledku poradiačního poškození slinných žláz a horního GIT

5y, 10y-lokální & distanční kontrola **77%**

časná, pozdní toxicita G3/4 **71%** resp. **35%**

## **N-status**

- N1-2a vs N2b-3 HR 2,3 (p=0,033), N1-2c vs N3 HR 2,5 (p=0,017)

## **Komorbidity**

- ACE-28 0-1 vs 2-3 HR 2,6 (p=0,006)

## **Kouření**

- nekuřák/exkuřák >5y vs nikotinismus HR 6,2 (p=0,016)



# Děkuji za pozornost

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