We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

172,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Update on Medical Therapies of Nasopharyngeal Carcinoma

Soumaya Labidi, Selma Aissi, Samia Zarraa,
Said Gritli, Majed Ben Mrad,
Farouk Benna and Hamouda Boussen
*Faculty of Medicine of Tunis,
University of Tunis
Tunisia*

1. Introduction

Nasopharyngeal carcinoma (NPC) is a common head and neck cancer in most of the countries of the Mediterranean Area (MA) and North Africa (NA). Its incidence is variable from <1 in sporadic areas to 2-7/100000 in NA and MA to 20-30/100000 in Southern China and Southeast Asia (Boussen et al, 2010; Lee et al, 1992). It's different from other head and neck cancers due to its particular epidemiology, natural history and therapeutic considerations (Boussen et al, 2010; Lee et al, 1992).

It's highly radiosensitive and chemosensitive. Loco-regional radiotherapy (RT) remains the primary treatment for early stage disease (T1-T2, N0, N1), while combined chemotherapy-radiotherapy became the gold therapeutic standard in locally advanced disease i.e T3-T4, N2-N3 (Boussen et al, 2010; Lee et al, 1992; Baujat et al, 2006). Combined treatment leads to a significant improvement on overall and disease-free survivals, but NPC remains at a high metastatic risk, requiring the search for new salvage therapeutic protocols (Boussen et al, 2010; Lee et al, 1992; Xu et al, 2010). This paper will focus on recent data on epidemiology and progresses on medical therapies in NPC.

2. Transitional epidemiology of NPC

NPC represents 2 to 5% of all cancers in males, it is second to laryngeal cancer in most of the Mediterranean countries and its incidence varying from 1 in Lebanon, Egypt, Greece, Turkey to 2-5/100000 in North Africa (NA), where it's characterized by a bimodal age repartition with a first peak at adolescence (Boussen et al, 2010; Ben Abdallah M, 2010). This high frequency of children and adolescents affected by NPC in Tunisia open the discussion to reach the maximum cure rate with minimal late aftereffects (Boussen et al, 2010). Endemic NPC is highly frequent in south-east Asia with an incidence > 20/100000 compared to NA (Tse et al, 2006). During the last 10 years, authors from Singapore reported a decrease of NPC incidence especially for UCNT type. This epidemiologic transition could be attributed to a socio-economic level increase as well as diet modification, such as salted fish (rich in nitrosamines) consumption decrease (Tse et al, 2006). The same trend have been observed

(Sun et al,2005) from 1992 to 2002 for the incidence Rates of NPC among Chinese Americans Living in Los Angeles County and the San Francisco Metropolitan Area with a decrease of 37% for men by 37% and only 1% in women(7). Conversely, male and female NPC world age-standardized incidence reported to be 27.5/105 and 11.3/105 respectively, seems to be stable from 1970-2007 in the Chinese endemic area of Zhongshan (Wei et al, 2010). In Tunisia (Ben Abdallah M,2010), we are observing, like in Singapore, a decreasing incidence of NPC and a projection from the North Tunisia cancer registry for 2024 suggests a significant drop of NPC incidence, while breast and colon cancer will clearly increase.

3. Staging and classification

During the last 20 years, NPC natural history became more known in term of loco-regional extension as well as metastatic disease with technical improvements of flexible nasofibrosopes and modern imagery, such as magnetic resonance imagery and Pet-scan(Chan et al,2011). This better definition of loco-regional disease extension leads to successive actualizations (1997, 2002 then 2009), of the more used TNM UICC anatomo-clinical classification, more adapted to discriminate between the different T and N prognostic stages and eventually to adjust therapeutic protocols according to risk group (Union for International Cancer Control,2009).

T1 Nasopharynx, oropharynx or nasal cavity (**was T2a***) without parapharyngeal extension

T2 Parapharyngeal extension (**was T2b***)

T2a Tumour extends to oropharynx and/or nasal cavity without parapharyngeal extension

T2b Tumour with parapharyngeal extension

T3 Bony structures of skull base and/or paranasal sinuses

T4 Intracranial, cranial nerves, hypopharynx, orbit, infratemporal fossa/masticator space

N1 Unilateral **cervical**, unilateral or bilateral retropharyngeal lymph nodes, above supraclavicular fossa; < 6 cm

N2 Bilateral **cervical** above supraclavicular fossa; < 6 cm

N3 Metastasis in lymph node(s), >6 cm in dimension (N3a) or in the supraclavicular fossa (N3b)>6 cm

7th TNM classification of UICC (International Union against Cancer, 2009)-AJCC, American Joint Committee on Cancer. *Recent modification

4. Chemotherapy

Systemic chemotherapy (CT) in NPC is indicated because disease is confined to nasopharynx in < 10% of cases (Lee et al; 1992), while parapharyngeal extension, skull base and intracranial involvement are reported in 80% and 25 to 35% and pathologic cervical nodes are present in 75 to 90% of patients, increasing the risk of initial metastases in advanced stages (Lee et al;1992; Sham et al,1991; Teo et al,1992). CT have been used since the eighties in palliative intent with few devoted phase II trials and the most active agents are

cisplatin, 5-fluorouracil (5-FU), doxorubicin, epirubicin, bleomycin, mitoxantrone, methotrexate and vinca alkaloids or more recently ifosfamide or gemcitabine (Bensouda et al, 2011; Boussen et al, 2010; You et al, 2011). CT have been used from the nineties as adjuvant then primary CT (PCT) in NPC (Bachouchi et al, 1990) confirming the chemosensitivity of NPC with a high rate of radiologic/endoscopic objective responses to PCT (Bachouchi et al, 1990; Ekenel et al, 2011).

5. Radiotherapy

RT remains is the mainstay of of NPC treatment due to its radiosensitivity (Boussen et al, 2010; Chan et al, 2010; Lee et al, 1992). Loco-regional RT targets primary tumor, its regional extension and both neck sides (levels Ib-V, and retropharyngeal nodes). Consensual dose is around 70 Gy with dose-fractions of 1.8 to 2Gy, indicated for sterilization of bulky tumor volume and 50-60 Gy or 46-60 Gy for areas at high risk (Lee et al, 1992; Chan et al, 2010).

6. Concomitant CT-RT

The results of concurrent chemoradiotherapy (CCRT) Intergroup study 0099, made gradually this combined approach as a standard in the treatment of patients with stage III and IV NPC (Al Sarraf et al, 1998; Chan et al, 2010). Within the randomized other studies, several meta-analysis and a pooled data analysis reported a significant improvement of survival in NPC patients treated by CT-RT versus RT alone (Baujat et al, 2006). The NPC meta-analysis had shown the superiority of concomitant scheme vs neoadjuvant chemotherapy. It concerned 1753 patients with N1> 2cm, N2> 3cm, N3, T4, PS 0- 1, WHO 2- 3 and a mean age of 46 years. The follow-up was < 5 years for 2 trials (299 pts), 5-9 years for 6 (1454 pts) and a median follow-up of 6 years for the whole population. Delivered radiotherapy were for tumor: 65-74 Gy, for N0 : 50-66 Gy and for N+ 60-76 Gy, by using a "classical" technique and a boost for residual N associated to concomitant cisplatin-based CT in all trials. Authors reported a benefit of concomitant scheme by increasing 5-year OS from 56% to 62% and EFS from 42% to 52% significantly better than neoadjuvant chemotherapy. Recently a meta-analysis focused on South East Asian phase III trials of CT-RT from the NPC endemic area. 1608 patients were collected from seven trials (Zhang L et al, 2010) and they reported Risk ratios (RRs) of 0.63 (95% CI, 0.50 to 0.80), 0.76 (95% CI, 0.61 to 0.93) and 0.74 (95% CI, 0.62 to 0.89) for 2, 3 and 5 years OS respectively in favor of the CCRT group. Concerning the 3-years absolute number of locoregional recurrence rate (LRR), a significant overall benefit in favor of the addition of chemotherapy was found with RR of 0.67 (95% CI, 0.49 to 0.91). A significant decrease of metastatic risk was also observed in term of 3-years absolute number of distant metastasis rate (DMR) with a RR of 0.71. The RRs were larger than that detected in the previously reported meta-analysis (including both endemic and non-endemic), and authors concluded that "the relative benefit of CCRT in endemic population might be less than that from previous meta-analyses".

6.1 CT Protocols of concomitant CT-RT

The schemes used for CT-RT are mainly based on "Al Sarraf" schedule with Cisplatin 100mg/m², every 3 weeks on D1,22,43 or weekly Cisplatin at 40mg/m² (Chan Scheme),

who’s the most frequently used in MA and NA, while radiotherapy doses is usually $\geq 66\text{Gy}$ ($1.8\text{-}2\text{Gy/Fx/d}$, 5Fx/wk) for primary nasopharyngeal tumor and its extensions + additional boosts to the parapharyngeal space, the primary or nodal sites not exceeding 20Gy . Since 10 years, CCRT is now recognized and applied as the better therapeutic approach for locally advanced NPC (Al Sarraf,1998 ; Chan et al,2010).

6.2 Acute and late toxicities of CT-RT

CT-RT compared to PCT, however increased significantly acute grade 3-4 toxicity at the end of combined treatment i.e mucositis, radiodermitis, dysphagia and consequently severe weight loss (WL) in most of the open or randomized studies (Table 1). This acute toxicity reduced considerably the compliance of weekly concomitant cisplatin, that was administered during the 6 weeks of CT-Rt in 94%,88%,74%,35%,7% and 3% for weeks 1 to 6 in Hui study (Hui et al,2009). The frequency of severe WL > 5-10% is probably underestimated by many authors and requires sometimes nasal tube feeding or parenteral nutrition as well as delay in the planned protocol. In a Chinese study (Qiu et al, 2011), of patients treated by CT-RT for NPC, 56% had at baseline, a mean 5% WL evaluated at 6.9 Kg after CT-RT (range 2.1-12.6 kg). Xerostomia is one of the most frequent sequelae after salivary gland irradiation and Intensity-Modulated RT permits to reach a high tumor control rate, but also to reduce severity and frequency of xerostomia (Lee et al, 2009).

Author/year	Hui/2010		Lee/2010		Zheng/2010	
After PCT	An	---	--		1.7%	
	Neutr	97%	--		6.8%	
	Thr	--	--		--	
	N/V	8.8%	--		5.1%	
After CT-RT	An	8.8	19.2	19	1	39%
	Neutr	26.4	15.3	32%	1%	35.6%
	Thr			2%	0%	
	Mucos	23.5	7.7	61%	48%	---
	N/V	8.8	7.7	18%	1%	47.1%
	WL			27%	27%	
	Rad			20%	16%	
Late toxicities	Dys	---	3.8%	1%	0%	3.4%
	Xer	32.4	30.8%	---	---	91.5%
	Skin	11.8	19.2%	4%	5%	
	Subc	20.6	11.5%			
	HL	8.8	11.5%	6%	---	3.4%
	Otit			21	15%	3.5%
	Hypoth			8%	6%	6.8%
	SC	5.9	3.8%			

Table 1. Acute and late toxicities after CT-RT.

Despite many technical advances in RT, late toxicities i.e mainly xerostomia, cervical subcutaneous fibrosis, trismus, hearing loss of less frequently second cancers are observed decreasing the Quality of Life of long-term survivors from NPC, specially those treated in childhood or adolescence (Boussen et al,2010; Xiao et al,2011).

6.3 What next after concomitant CT-RT?

After the era of exclusive CT-RT, appeared the next generation protocols associating PCT followed by CT-RT (Fountzilas et al, 2011, Hui et al, 2009). PCT protocols included “classical” 5FU-cisplatin, anthracyclin-cisplatin or more recently taxanes-cisplatin associations (Table 2). Hui and al, reported their results on 65 patients treated cisplatin-docetaxel (DC) protocol followed by CCRT vs CCRT alone. They observed a significant survival benefit at 2 years for the DC arm (93% vs 76%, *p* = .013). Others studies including also taxanes, showed a benefit for overall and disease-free survival of patients treated for NPC in MA are currently varying from 66 to 94% and 63 to 88.2% (table 3). Many of these studies have a short Follow-up, but OS and DFS rates seems to be promising probably better than those reported in exclusive CT-RT. In Tunisia, a prospective GORTEC French trial is ongoing, comparing 2 cycles of primary TPF followed by chemoradiotherapy vs CCRT with weekly cisplatin (40mg/ m2) in advanced(N2-3, T3-4).

Author/year	Nb	CT	RT	ORPCT	ORCT-RT	OS/DFS
Zheng/2010	60	Ned/FU Ned Conc	IMRT 70/55-60	-----	95.3%	3 yr 85.5/75%
Fountzilas	72	CPE-CRT	66-70/50-66	70%	83%	3 yr 66.6/64.5
2011	69	CRT	-----	-----	85%	3 yr 71.8/63.5
Hui	34	DC-CRT	70/50-60	76,5%	97.1%	3 yr 94.1/88.2%
2009	31	CRT	70/50-60	----	100%	3 yr 69.2/63%

CPE :Cisplatin-Paclitaxel-Epirubicin, DC : Docetaxel-cisplatin, CRT : Concomitant chemo-radiotherapy, Ned : Nedaplatin.

Table 2. Therapeutics results of open or randomized studies of PCT followed by CT-RT.

7. Tumor volume in NPC: A new prognostic factor?

Instead of the classical T,N,Age,Sex and histologic type, prognostic value of Primary Tumor Volume(PTV), measured by CT-scan have been explored for NPC in 112 patients with Stage I-IVB NPC treated by IMRT (Chen et al, 2011). The mean PTV was 33.9 ± 28.7 ml and classified from V1 to V4 (from 15.65 to 50,5ml). It impacted on 5-year overall survival who varies from 88.5, 83.3, 82.4 to 54.5% for V1 to V4 from, showing that V1-V4 are clearly separated from V4 (*p* = 0.014). Cox proportional hazards regression model analysis showed that a PTV >50 ml was an independent risk factor for radiotherapy (risk ratio = 3.485, *P* = 0.025). In 56 Turkish patients with locally advanced NPC, PTV have been calculated by measuring tumor diameters by CT and MR film hardcopies computed as an ellipsoid ($V=4/3 \pi \cdot d1 \cdot d2 \cdot d3$) to obtain the diameter-based volume(Sarisahin et al, 2011). They reported in the monovariate analysis, that primary tumor volume have a significant predictive value on DFS and DMFS, if tumor volume < 20ml, DFS was 60% vs 0% if > 60ml(*p*=0.007). The residual tumor volume (RTV) at first control after treatment was also

found to be a significant prognostic factor on LRRFS ($p=0.03$). However Nasopharyngeal PTV alone is missing the volume of satellite cervical nodes that have probably an important prognostic value.

8. Recurrent/metastatic disease

NPC failures are mainly metastatic, to bones, lungs and liver and loco-regional relapses became more rare due to the high loco-regional control rate obtained by loco-regional RT (Leung et al,2005; Cvitkovic et al,1993). In metastatic situations, NPC remains chemosensitive to cisplatin, adriamycin, 5Fluorouracil or more recently taxanes, gemcitabine or oral capecitabine(Boussen et al,1991,2010;You et al,2011;Bensouda et al,2011). Prolonged survival after palliative CT and/or RT could be observed in patients with bone metastases in case of bone MTS only and less than 4 sites involved (Fandi et al,2000;Cao et al,2011). In isolated bone metastases, prolonged responses under biphosphonates plus CT have been also reported, with a significant reduction of skeletal events and better (11.5 vs 5.5 months, $P < 0.001$) progression-free survival and overall survival (23.5 vs. 17.5 months, $P < 0.001$) of combined vs chemotherapy alone group. (Jin et al,2011). Even in case of lung MTS disease, different prognostic groups could be identified according to size and numbers of metastatic nodules (Cao X et al, 2011).

9. Effective screening for NPC?

Some efforts have been done oriented for early detection in relatives of patients considered at high risk for NPC, according to their viral DNA and anti-EBV profile (Baizig et al,2011;Liu et al,2011). Sophisticated endoscopic technique have been also tested to detect easily early stages of NPC (Lin et al,2011, Lin et al,2011).

10. Conclusion

NPC is a very interesting within the other head and neck cancers, occurring in young patients non-smokers/non drinkers and significant improvement of therapeutic results have been reached during the last 30 years, 5 years-OS increasing from 20-30% to more than 75% with the recent protocols of CT-RT or PCT followed by CT-RT that included taxanes (Boussen et al, 2010, Chan et al,2010). Overexpression of EGFR, present in more than 70% of NPC leads to the use of Cetuximab as adjuvant concomitant or maintenance therapy (Yang Y et al, 2011). Anti-angiogenesis therapies like Pazopanib have been also tested without proven efficacy(Lim et al,2011). The significant survival improvement made NPC a more curable disease and efforts were made to reduce late sequelae specially in children and adolescents and to affect minimally quality of life after combined chemo-radiotherapy (Fang et al,2011;Marucci et al,2011;Shueng et al,2011).

11. References

Al-Sarraf M, LeBlanc M, Giri PG et al. (1998).Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: phase III randomized Intergroup study 0099. *J Clin Oncol*,16,1310-1317.

- Bachouchi M, Cvitkovic E, Azli N et al. (1990). High complete response in advanced nasopharyngeal carcinoma with bleomycin, epirubicin, and cisplatin before radiotherapy. *J Natl Cancer Inst* 1990,82,7,(April 1990):616-20.
- Baizig NM, Morand P, Seigneurin JM, Boussen H et al. (2011). Complementary determination of Epstein-Barr virus DNA load and serum markers for nasopharyngeal carcinoma screening and early detection in individuals at risk in Tunisia. *Eur Arch Otorhinolaryngol* (Jul 2011).
- Baujat B, Audry H, Bourhis J et al. (2006). MAC-NPC Collaborative Group. Chemotherapy in locally advanced nasopharyngeal carcinoma: an individual patient data meta-analysis of eight randomized trials and 1753 patients. *Int J Radiat Oncol Biol Phys*,64,1, (January 2006),47-56.
- Ben Abdallah M. (2010). North Tunisia Cancer Registry. Data for 2003-2007. Institut Salah Azaiz. Tunis.
- Bensouda Y, Kaikani W, Ahbeddou N et al. (2011). Treatment for metastatic nasopharyngeal carcinoma. *Eur Ann Otorhinolaryngol Head Neck Dis*,128,2,(Apr 2011),79-85.
- Boussen H, Cvitkovic E, Wendling JL, Azli N, Bachouchi M, Mahjoubi R, Kalifa C, Wibault P, Schwaab G, Armand JP. (1991). Chemotherapy of metastatic and/or recurrent undifferentiated nasopharyngeal carcinoma with cisplatin, bleomycin, and fluorouracil. *J Clin Oncol* 9,9,(Sep 1991),1675-81.
- Boussen H, Bouaouina N, Daldoul O, Benna F, Gritli S, Ladgham A. (2010). Update on medical therapies of nasopharyngeal carcinomas. *Bull Cancer*,97,4,(April 2010),417-26.
- Cao X, Han Y, He L, Xiang J, Wen Z.(2011). Risk subset of the survival for nasopharyngeal carcinoma patients with bone metastases: who will benefit from combined treatment? *Oral Oncol*,47,8,(August 2011),747-52.
- Chan AT, Teo PM, Ngan RK et al. (2002). Concurrent chemotherapy-radiotherapy compared with radiotherapy alone in locoregionally advanced nasopharyngeal carcinoma: progression-free survival analysis of a phase III randomized trial. *J Clin Oncol*,20,2038-2044.
- Chan ATC, Grégoire V, Lefebvre JL, Licitra L, Felip E(2010).Nasopharyngeal cancer: EHNS-ESMO ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up; *Ann Oncol*,21,(suppl 5): v187-v189.
- Chen C, Fei Z, Pan J, Bai P, Chen L et al. (2011). Significance of primary tumor volume and T-stage on prognosis in nasopharyngeal carcinoma treated with intensity-modulated radiation therapy. *Jpn J Clin Oncol*,41,537-42.
- Chan SC, Chang JT, Lin CY et al(2011). , Ng SH, Wang HM, Liao CT, Chang CJ, Lin SY, Yen TC. Clinical utility of 18F-FDG PET parameters in patients with advanced nasopharyngeal carcinoma: predictive role for different survival endpoints and impact on prognostic stratification. *Nucl Med Commun*, (August 2011).
- Cvitkovic E, Bachouchi M, Boussen H, Busson P, Rousselet G, Mahjoubi R, Flores P, Tursz T, Armand JP, Azli N.(1993). Leukemoid reaction, bone marrow invasion, fever of unknown origin, and metastatic pattern in the natural history of advanced undifferentiated carcinoma of nasopharyngeal type: a review of 255 consecutive cases. *J Clin Oncol*,11,12,(Dec 1993),2434-42.

- Ekenel M, Keskin S, Basaran M, Ozdemir C, Meral R, Altun M, Aslan I, Bavbek SE. Induction chemotherapy with docetaxel and cisplatin is highly effective for locally advanced nasopharyngeal carcinoma. *Oral Oncol* 2011 Jul;47(7):660-4.
- Fandi A, Bachouchi M, Azli N, Taamma A, Boussen H, Wibault P, Eschwege F, Armand JP, Simon J, Cvitkovic E.(2000). Long-term disease-free survivors in metastatic undifferentiated carcinoma of nasopharyngeal type. *J Clin Oncol* 18,6,(Mar 2000),1324-30.
- Fang FM, Tsai WL, Lee TF, Liao KC, Chen HC, Hsu HC.(2010). Multivariate analysis of quality of life outcome for nasopharyngeal carcinoma patients after treatment. *Radiother Oncol*,97,2, (Nov 2010),263-9.
- Fountzilas G, Ciuleanu E, Bobos M et al. (2011). Induction chemotherapy followed by concomitant radiotherapy and weekly cisplatin versus the same concomitant chemoradiotherapy in patients with nasopharyngeal carcinoma: a randomized phase II study conducted by the Hellenic Cooperative Oncology Group (HeCOG) with biomarker evaluation. *Ann Oncol* Apr 27.
- Gao F, Wee J, Wong HB, Machin D. (2010). Quality-of-life-adjusted survival analysis of concurrent chemo radiotherapy for locally advanced (nonmetastatic) nasopharyngeal cancer. *Int J Radiat Oncol Biol Phys*,78,454-60.
- Hui EP, Ma BB, Leung SF et al. (2009). Randomized phase II trial of concurrent cisplatin radiotherapy with or without neoadjuvant docetaxel and cisplatin in advanced nasopharyngeal carcinoma. *J Clin Oncol* 2009;27:242-9.
- Jin Y, An X, Cai YC, Cao Y, Cai XY, Xia Q, Tan YT, Jiang WQ, Shi YX. Zoledronic acid combined with chemotherapy bring survival benefits to patients with bone metastases from nasopharyngeal carcinoma. *J Cancer Res Clin Oncol* 2011 Aug 13.
- Lee N, Harris J, Garden AS et al.(2009). Intensity-modulated radiation therapy with or without chemotherapy for nasopharyngeal carcinoma: radiation therapy oncology group phase II trial 0225. *J Clin Oncol* 27,22,(August 2009),3684-90.
- Lee AW, Poon YF, Foo W et al. (1992). Retrospective analysis of 5037 patients with nasopharyngeal carcinoma treated during 1976-1985: overall survival and patterns of failure. *Int J Radiat Oncol Biol Phys*,23,2,261-70.
- Lee AW, Tung SY, Chua DT et al. (2010). Randomized trial of radiotherapy plus concurrent-adjuvant chemotherapy vs radiotherapy alone for regionally advanced nasopharyngeal carcinoma. *J Natl Cancer Inst*,102,15,(Aug 2010),1188-98.
- Leung TW, Tung SY, Sze WK et al.(2005) Treatment results of 1070 patients with nasopharyngeal carcinoma: an analysis of survival and failure patterns. *Head Neck*,27,555-65.
- Lim WT, Ng QS, Ivy P et al. (2011). Tan A Phase II Study of Pazopanib in Asian Patients with Recurrent/Metastatic Nasopharyngeal Carcinoma. *Clin Cancer Res*,17,16,(Aug 2011),5481-9.
- Lin B, Bergholt MS, Lau DP, Huang Z. (2011). Diagnosis of early stage nasopharyngeal carcinoma using ultraviolet autofluorescence excitation-emission matrix spectroscopy and parallel factor analysis. *Analyst*,136,19,(Oct 2011),3896-903.
- Lin YC, Wang WH. Narrow-band imaging for detecting early recurrent nasopharyngeal carcinoma. (2011). *Head Neck*,33,4,(April 2011)591-4.
- Liu Y, Huang Q, Liu W et al. (2011). Establishment of VCA and EBNA1 IgA-based combination by enzyme-linked immunosorbent assay as preferred screening

- method for nasopharyngeal carcinoma: A two-stage design with a preliminary performance study and a Mass screening in southern china. *Int J Cancer*, (Aug 2011).
- Marucci L, Marzi S, Sperduti I, Giovinazzo G, Pinnarò P, Benassi M, Strigari L. (2011). Influence of intensity-modulated radiation therapy technique on xerostomia and related quality of life in patients treated with intensity modulated radiation therapy for nasopharyngeal cancer. *Head Neck*, (Mar 2011).
- Qiu C, Yang N, Tian G, Liu H. (2011). Weight loss during radiotherapy for nasopharyngeal carcinoma: a prospective study from northern china. *Nutr Cancer*, 63, 6, (Aug-Sep 2011), 873-9.
- Sham JS, Choy D. (1991). Prognostic value of paranasopharyngeal extension of nasopharyngeal carcinoma on local control and short-term survival. *Head Neck*, 13, 298-310.
- Shueng PW, Shen BJ, Wu LJ, Liao LJ, Hsiao CH, Lin YC, Cheng PW, Lo WC, Jen YM, Hsieh CH. (2011). Concurrent image-guided intensity modulated radiotherapy and chemotherapy following neoadjuvant chemotherapy for locally advanced nasopharyngeal carcinoma. *Radiat Oncol*, 13, 6 (August 2011), 95.
- Sun LM, Epplein M, Li CI, Vaughan TL, Weiss NS. (2005). Trends in the Incidence Rates of Nasopharyngeal Carcinoma among Chinese Americans Living in Los Angeles County and the San Francisco Metropolitan Area, 1992-2002. *Am. J. Epidemiol*, 162, 12, (December 2005), 1174-1178.
- Teo P, Shiu W, Leung SF, Lee WY (1992). Prognostic factors in nasopharyngeal carcinoma investigated by computer tomography--an analysis of 659 patients. *Radiother Oncol*, 23, 79-93.
- Tse LA, Yu ITS, Mang OWK, Wong SL. (2006). Incidence rate trends of histological subtypes of nasopharyngeal carcinoma in Hong Kong. *Br J Cancer*, 95, 9, (Nov 2006), 1269-1273.
- Wei K, Xu Y, Liu J, Zhang W, Liang Z. (2010). No incidence trends and no change in pathological proportions of nasopharyngeal carcinoma in Zhongshan in 1970-2007. *Asian Pac J Cancer Prev*, 11, 6, 1595-9.
- Xiao WW, Huang SM, Han F, Wu SX, Lu LX, Lin CG, Deng XW, Lu TX, Cui NJ, Zhao C. (2011). Local control, survival, and late toxicities of locally advanced nasopharyngeal carcinoma treated by simultaneous modulated accelerated radiotherapy combined with cisplatin concurrent chemotherapy: long-term results of a phase 2 study. *Cancer*, 117, 9, (May 2011), 1874-83.
- Xu L, Pan J, Wu J, Pan C, Zhang Y, Lin S, Yang L, Chen C, Zhang C, Zheng W, Lin S, Ni X, Kong FM. (2010). Factors associated with overall survival in 1706 patients with nasopharyngeal carcinoma: significance of intensive neoadjuvant chemotherapy and radiation break. *Radiother Oncol*. , 96, 1, (July 2010), 94-9.
- TNM Classification of malignant tumors. 7th edition. Union for International Cancer Control. (2009). Geneva. <http://www.uicc.org/node/7735>.
- Xiao WW, Huang SM, Han F et al. (2011). Local control, survival, and late toxicities of locally advanced nasopharyngeal carcinoma treated by simultaneous modulated accelerated radiotherapy combined with cisplatin concurrent chemotherapy: long-term results of a phase 2 study. *Cancer* 2011 May 1; 117(9):1874-83.
- Yang Y, Xuan J, Yang Z, Han A, Xing L, Yue J, Hu M, Yu J. (2011). The expression of epidermal growth factor receptor and Ki67 in primary and relapse nasopharyngeal

- cancer: a micro-evidence for anti-EGFR targeted maintenance therapy. *Med Oncol*, 2011 Jul 23.
- You B, Le Tourneau C, Chen EX et al. A Phase II Trial of Erlotinib as Maintenance Treatment After Gemcitabine Plus Platinum-based Chemotherapy in Patients With Recurrent and/or Metastatic Nasopharyngeal Carcinoma. (2011). *Am J Clin Oncol* 2011 Feb 22.
- Zhang L, Zhao C, Ghimire B et al. (2010). The role of concurrent chemoradiotherapy in the treatment of locoregionally advanced nasopharyngeal carcinoma among endemic population: a meta-analysis of the phase III randomized trials. *BMC Cancer*, (October 2010), 10, 558.
- Zheng J, Wang G, Yang GY, Wang D, Luo X, Chen C, Zhang Z, Li Q, Xu W, Li Z, Wang D. Induction chemotherapy with nedaplatin with 5-FU followed by intensity-modulated radiotherapy concurrent with chemotherapy for locoregionally advanced nasopharyngeal carcinoma. *Jpn J Clin Oncol*, 40, 5 (May 2010), 425-31.

IntechOpen

Carcinogenesis, Diagnosis, and Molecular Targeted Treatment for Nasopharyngeal Carcinoma

Edited by Dr. Shih-Shun Chen

ISBN 978-953-307-867-0

Hard cover, 246 pages

Publisher InTech

Published online 15, February, 2012

Published in print edition February, 2012

This book is a comprehensive treatise of the potential risk factors associated with NPC development, the tools employed in the diagnosis and detection of NPC, the concepts behind NPC patients who develop neuro-endocrine abnormalities and ear-related complications after radiotherapy and chemotherapy, the molecular mechanisms leading to NPC carcinogenesis, and the potential therapeutic molecular targets for NPC.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Soumaya Labidi, Selma Aissi, Samia Zarraa, Said Gritli, Majed Ben Mrad, Farouk Benna and Hamouda Boussen (2012). Update on Medical Therapies of Nasopharyngeal Carcinoma, Carcinogenesis, Diagnosis, and Molecular Targeted Treatment for Nasopharyngeal Carcinoma, Dr. Shih-Shun Chen (Ed.), ISBN: 978-953-307-867-0, InTech, Available from: <http://www.intechopen.com/books/carcinogenesis-diagnosis-and-molecular-targeted-treatment-for-nasopharyngeal-carcinoma/update-on-medical-therapies-of-nasopharyngeal-carcinoma-npc->

INTECH
open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](https://creativecommons.org/licenses/by/3.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen