

SKIN CANCER

Etiology

- High insolation.
- Long-term contact with chemical carcinogens — products of oil refining, coal, shale oils, arsenic combinations.
- Ionizing radiation,
- Constant skin injuries (mechanical injuries, burns).

Pathomorphology

- Basal-cell (basalioma).
- Squamous cell carcinoma (keratinized and non-keratinized).

Epidemiology

- Bulgaria — the sickness rate is 36 per 100,000 of population.
- England — 1.9 per 100,000 of population.

. Ukraine — 35—38 per 100,000 of population.

It is observed that countrymen are more likely to have skin cancer than city dwellers.

Facultative precancerous forms:

- skin horn (Fig. 83);
- keratosis (Fig. 82);
- senile skin atrophy;
- atheroma;
- deep skin mycosis;
- keratoacanthoma;
- papilloma;
- red flat herpes.

Obligate precancerous forms:

- Bouen tumor (Fig. 84);
- xeroderma pigmentosum;
- Cair disease.

TNM staging of skin cancer (Table 2)

Primary tumor

- TX — not enough evidence for the primary tumor.
- TO — the primary tumor is not identified.
- Tis — carcinoma in situ.
- T1 — the tumor is 2 cm in the greatest dimension.
- T2 — the tumor is > 2 cm, but < 5 cm in the greatest dimension.
- T3 — the tumor is > 5 cm in the greatest dimension.
- T4 — the tumor grows into the lower organs (cartilages, muscles, bones).

Regional lymph node involvement

- Nx — not enough evidence for regional lymph nodes evaluation.
- > NO — no evidence of regional lymph nodes affection.
- N1 — the regional lymph nodes are affected.

Metastatic involvement

- Mx — not enough evidence to identify distant metastasis.
- MO — distant metastasis is not identified.
- M1 — there is distant metastasis.

table 2. **Skin cancer staging**

| | | | |
|-----------|------|------|----|
| Stage 0 | Tis | NO | MO |
| Stage I | T1 | NO | MO |
| Stage II | T2 | NO | MO |
| | T3 | NO | MO |
| Stage III | T4 | NO | MO |
| | AnyT | N1 | MO |
| Stage IV | AnyT | AnyN | M1 |

Clinical forms (Fig. 85—92):

- superficial;
- infiltrative or deep-penetrative;
- papillary.

Diagnostics

- Examination.
- Palpation.
- .Dermatoscopy.
- Cytological analysis of the scrape, smear.
- Incisional biopsy.
- Sonography — to diagnose metastases in regional lymph nodes.
- Inspection of the distant metastases, radiography of the thoracic cavity **organs and** ultrasonography of the abdominal cavity.

Differential diagnostics

- Red Lupus.
- Tuberculosis.
- Syphilitic gumma.
- Actinomycosis.
- Melanoma.
- Non-malignant skin growths.

Basal-cell skin cancer treatment

- *Electroexcision* (recovery takes place in 95 % cases).
- *Closely-focused* radiotherapy (recovery takes place in 90 % cases).
- *Excision* (recovery takes place in 95 % cases).
- *Cryotherapy*.
- m Relapse is treated by *wide excision*.

Squamous cell carcinoma treatment

- *Surgery* (Stage I, II) — wide ablation of the tumor with the healthy skin area around it (not less than 2 cm) together with the hypodermic cellular tissue and fascia.
- *Radiotherapy* (Stage I, II) (closely-focused radiotherapy, total dose is

30—60 Gr).

- *Medicines* (Stage III, IV) (chemotherapy).

Prognosis

- In case of regional lymph nodes metastases absence 5-year survival is guaranteed in 75—80 % cases, and when the disease is diagnosed early almost 80—100 % patients completely recover and do not have relapses.
- 5-year survival with regional lymph nodes metastases and growing through adjacent organs and tissues is only 24 %.

Non-malignant skin tumors of conjunctive tissue origin

- Fibroma (soft and hard).
- Dermatofibroma.
- Lipoma.
- Angioma.
- Gemangioendotelioma.
- Neurofibroma.

The treatment used here is surgical.

Skin sarcomas (histological classification)

- Tumors of the formed dense conjunctive fibrous tissue (fibrosarcoma and dermatosarcoma Darie).
- Tumors of the fat base (liposarcoma).
- Tumors of the muscle tissue (miosarcoma).
- Tumors of the blood and lymphatic vessels (angiosarcoma, angioendotelioma, Kaposi's sarcoma, lymphangiosarcoma).
- Tumors of undifferentiated cells (undifferentiated sarcoma, mixosarcoma).

Skin sarcoma treatment

- Surgical.
- Closely-focused radiotherapy with corticosteroids.
- In cases of generalized forms of Kaposi's sarcomas cytostatic therapy is used — the combination of doxorubicin, vinblastin, and bleomicin, and also monochemotherapy with prospidin.
- Ss biotherapy intron A is used.

Skin melanoma etiology

Exogenous risk factors

- *Physical factors*: ultra-violet solar radiation, ionizing radiation, electromagnetic radiation, fluorescence radiation; nevus traumatism.
- *Chemical factors*: harmful chemical agents used in petrochemical, chemical (in particularly producing nitric acid), rubber-producing plants, in the production of vinyl chloride, polyvinyl chloride, plastic, benzol, pesticides.
- *Biological factors*: nutrition quality (high level of daily protein and

adipose consumption), medical products (exogenous estrogens).

Endogenous risk factors

- u Biological constitution features, whose presence raises the risk for melanoma development: racial and ethnic predisposition, the level of body pigmentation, hereditary factors, anthropometric indexes, immune failings, endocrine factors, reproductive female factors.
- Predecessors of melanoma, that is such pathological skin changes, which can have the probability of malignant mutation: pigmentary parchment-skin, Dubrei melanosis, nevuses.

Melanoma pathomorphology

- Epithelial.
- Spindle-cell.
- Mixed.
- Small-cell.

TNM staging of skin melanoma (Table 3)

Primary tumor

- Tis — melanoma in situ.
- T1 — the tumor is less than 1 mm thick: a) without ulceration and the invasion level is II/III; b) with ulceration or the invasion level is IV/V.
- T2 — the tumor is 1.01—2.0 mm thick: a) without ulceration; b) with ulceration.
- T3 — the tumor is 2.01—4.0 mm thick: a) without ulceration; b) with ulceration.
- T4 — the tumor is more than 4 mm thick: a) without ulceration; b) with ulceration.

Regional lymph node involvement

- N1 — metastases in 1 gland: a) micrometastases 1; b) macrometastases 2.
- N2 — metastases in 2—3 lymph nodes: a) micrometastases 1; b) macrometastases 2; c) transitional metastases/satellites without metastatic lymph nodes.
- N3 — 4 and more metastatic lymph nodes or a conglomeration of lymph nodes, or transitional metastases/satellites with metastatic lymph nodes.

Micrometastases 1 are diagnosed after observation or selective lymphodenectomy.

Macrometastases 2 are clinically found in lymph nodes, confirmed by therapeutical lymphodenectomy or extracapsular spread of metastases in the lymph nodes.

Metastatic involvement

- M1a — there are distant metastases on the skin, hypoderma or in the lymph nodes.
- M1b — metastases in the lungs.
- M1c — other visceral or any distant metastases.

The main signs of nevi malignization

- Disappearance of skin pattern from the nevus surface.
 - Appearance of shiny, glossy nevus surface.
 - Appearance of asymmetry or contours irregularity — scalloped contours of the nevus, i.e. changes of its shape.
 - Horizontal nevus growth.
 - Appearance of the subjective sensation of heat, itching or pain in the nevus area.
 - Appearance of single nodules (satellites) around the nevus.
-
- Appearance of single nodules on the surface of the nevus without its visual growth.
 - Peeling of the nevus surface with formation of withered "scabs".
 - Absence of hair or shedding of hair on the nevus surface.
 - Partial (irregular) or complete color change of the nevus-melanoma — appearance of areas of the so-called bound depigmentation.
 - Vertical growth of the nevus-melanoma.
 - Consistence change of the nevus-melanoma (detected by palpation) — its softening.
 - Ulceration of the epidermis above the nevus-melanoma.
 - Inflammation in the area of the nevus-melanoma and surrounding tissues.
 - Weeping of the nevus-melanoma surface.
 - Bleeding of the nevus-melanoma.

Clinical-anatomical forms of melanoma (Fig. 93—98)

- Superficial (70 %).
- Nodule-like (nodous, nodular; 15 %).
- Acral lentiginous and mucous melanoma (10 %).
- Lentigo maligna melanoma (melanoma-like freckles).

Melanoma diagnostics

- Studying:
 - anamnesis;
 - previous skin changes;
 - external tumor shape;
 - the state of the lymph nodes system. *m'~*
- Dermatoscopy.
- Echography.
- Tumor thermography.
- Cytological analysis of smears — tumor prints, sentinel node biopsy.
- Radioisotope scanning with the help of radio-active ^{32}P (300%).

Differential diagnostics of melanoma

- Youth melanoma (Spitz nevus).
- Blue nevus.
- Halo-nevus.
- Dysplastic nevus.
- Cavernous thrombotic hemangioma.
- Non-malignant skin tumors.

- Malignant skin tumors.
- Underungual and underepidermal hematoma.
- Onihomikosis.
- Extragenital chancre.
- Metastases of tumors of other histogenesis into skin.

Skin melanoma treatment

- Skin incision should be performed within the distance of 3—5 cm from the tumor, in this case it is necessary to step back in the direction of the regional lympho-outflow.
- It is necessary to ablate in one block the skin, hypodermic cellular tissue and fascia.
- The surgery should be necessarily performed with general anesthesia.
- When there is a suspicion of regional lymph nodes having metastases, regional lymphadenectomy should be performed at the same time.

Stage I treatment

- The standard treatment in case of IA and IB stages is wide excision of the tumor at the distance of 2 cm from the tumor borders.

Stage II treatment

- The standard excision is at the distance of 3 cm from the tumor borders.
- Besides tumor excision it is possible to perform immunotherapy using interferon a-2b 3 ml ME/m² of hypodermic injection 3 times per week during 3 years or until a relapse and melanoma metastases.

Stage III treatment

- The medical standard is wide excision of the primary tumor within 3 cm and more combined with regional lymphadenectomy.
- Chemotherapy (chemoimmunotherapy), immunotherapy (interferon a-2b, BCG), polychemotherapy should be performed in usual or modified (hyperthermia, hyperglycemia, etc.)

conditions. As polychemo therapy dacarbazine is used combined with platinum medications (cisplatin), periwinkle alkaloids (vinblastine), and medications of urea nitromesil group (lomustin).

Stage IV treatment

- The standard of this tumor treatment is systemic chemotherapy.
- The surgical treatment of stage IV melanoma can be performed in the presence of single metastases in the lungs, gastrointestinal tract, bones or brain. Palliative resections are done, which in some cases are very effective and prolong life significantly.
- Palliative radiotherapy can relieve the patient's state.
- In addition to main schemes of melanoma treatment it is common to use antiestrogens (tamoksifen).

Prognosis

- In case of localized process 5-year survival is possible in 75—86 % cases, 10-year — 47 %.

- In case of regional metastases — 33—52 % and 13 %
- * accordingly.
- In case of distant metastases 5-year survival does not exceed 5—12%.

LIP AND ORAL CAVITY CANCER

Anatomical regions

The oral cavity extends from the skin-vermilion junctions of the anterior lips to the junction of the hard and soft palates above and to the line of circumvallate papillae below and is divided into the following specific areas:

- Lip;
- anterior two thirds of tongue;
- buccal mucosa;
- floor of mouth;
- lower gingiva;
- retromolar trigone;
- upper gingiva;
- hard palate.

Spread

— The main routes of lymph node drainage are into the first station nodes:

- buccinator,
- jugulodigastric,
- submandibular,
- submental.

Sites close to the midline often drain bilaterally.

— Second station nodes include:

- parotid,
- jugular,
- upper and lower posterior cervical nodes.

Histological classification

- Most head and neck cancers are of the squamous cell variety and may be preceded by various precancerous lesions. An invasive carcinoma will be either well-differentiated, moderately differentiated, poorly differentiated or undifferentiated.
- Other tumors of the glandular epithelium, odontogenic apparatus, lymphoid tissue, soft tissue, and bone and cartilage origin require special consideration

Diagnosis

- Assessment of the primary tumor is based on inspection and palpation when possible and both indirect mirror examination and direct endoscopy when necessary.
- The tumor must be confirmed histologically, and any other pathologic data obtained by biopsy may be included.
- The appropriate nodal drainage areas are examined by careful palpation. Information from diagnostic imaging studies may be used in staging.
- Magnetic resonance imaging offers an advantage over computed tomographic scans in the detection and localization of head and neck tumors and in the distinction of lymph nodes from blood vessels.

TNM staging (Table 4)

Primary tumor

- TX: Primary tumor cannot be assessed.
- TO: No evidence of primary tumor.
- Tis: Carcinoma in situ.
- T1: Tumor < 2 cm in the greatest dimension.
- T2: Tumor > 2 cm but < 4 cm in the greatest dimension.
- T3: Tumor > 4 cm in the greatest dimension.
- T4: (lip) Tumor invades through the cortical bone, inferior alveolar nerve, mouth floor, or skin of face, Le. chin or nose.
- T4a: (oral cavity) Tumor invades adjacent structures (e.g. through the cortical bone, into the deep (extrinsic) muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), maxillary sinus, and skin of face).
- T4b: Tumor invades the masticatory space, pterygoid plates, or skull base and/or encases internal carotid artery

Note: Superficial erosion only of the bone/tooth socket by gingival primary is not sufficient to classify a tumor as T4. **Regional lymph node involvement**

- NX: Regional lymph nodes cannot be assessed.
 - N0: No regional lymph node metastases.
 - N1: Metastasis in a single ipsilateral lymph node, < 3 cm in the greatest dimension.
 - N2: Metastasis in a single ipsilateral lymph node > 3 cm but < 6 cm in the greatest dimension; or in multiple ipsilateral lymph nodes, < 6 cm in the greatest dimension; or in bilateral or contralateral lymph nodes < 6 cm in the greatest dimension.
 - N2a: Metastasis in a single ipsilateral lymph node > 3 cm but < 6 cm in the greatest dimension.
 - N2b: Metastasis in multiple ipsilateral lymph nodes < 6 cm in the greatest dimension.
 - N2c: Metastasis in bilateral or contralateral lymph nodes < 6 cm in the greatest dimension.
 - N3: Metastasis in a lymph node > 6 cm in the greatest dimension.
- Most masses > 3 cm in diameter are not single nodes but confluent nodes or tumors in soft tissues of neck. Midline nodes are considered homolateral nodes.

Metastatic involvement

- MX: Distant metastasis cannot be assessed.
- MO: No distant metastasis.
- M1: Distant metastasis.

Table 4. **Lip and oral cavity cancer staging**

| | | | |
|--------------------|-------------|--------------------|----------------|
| ■ Stage 0 | Tis, NO, MO | M Stage IVA | T4a, NO, MO |
| ■ Stage I | T1.N0, MO | | T4a, N1, MO |
| ■ Stage II | T2, NO, MO | | T1,N2,M0 |
| ■ Stage III | T3.N0, MO | | T2,N2,M0 |
| | T1.N1.MO | | T3, N2, MO |
| | T2,N1,M0 | | T4a, N2, MO |
| | T3, N1, MO | ■ Stage IVB | any T, N3, MO |
| | | | T4b, any N, MO |
| | | ■ Stage IVC | anyT.anyN.M1 |

Treatment:

- surgery alone (patients with tumor of the tongue require almost total glossectomy; more advanced lesions require segmental bone resection, hemimandibulectomy, or maxillectomy);
- radiation therapy alone:
 - external-beam radiation therapy;
 - > interstitial implantation;
- both modalities produces;
- combination of these.

Stage I treatment

Small lesions of the lip:

- surgery and radiation therapy produce similar cure rates, and the method of treatment is determined by the anticipated cosmetic and functional results.

Small anterior tongue lesions:

- wide local excision transorally + either surgery or radiation therapy (interstitial implantation alone or with external-beam radiation therapy).

Small lesions of the buccal mucosa:

- surgery + radiation therapy (including brachytherapy);
- larger T1 lesions may be treated by surgical excision with split-thickness skin graft or radiation therapy.

Small lesions of the floor of mouth:

- surgery + radiation therapy.

Small lesions of the lower gingiva:

- intraoral resection with or without a rim resection of bone and repaired with a split-thickness skin graft + radiation therapy.

Small tumors of the retromolar trigone:

- limited resection of the mandible + radiation therapy. Small lesions of the upper gingiva and hard palate:
 - surgical resection + postoperative radiation therapy.

Stage II treatment

Small lesions of the lip:

- surgery + radiation therapy (external-beam and/or interstitial techniques).

Small anterior tongue lesions:

- radiation therapy + surgery. Small

lesions of the buccal mucosa:

- radiation therapy + surgery. Small

lesions of the floor of mouth:

- surgery + radiation therapy. Small

lesions of the lower gingiva:

- intraoral resection with or without a rim resection of bone and repaired with a split-thickness skin graft + radiation therapy.

Small tumors of the retromolar trigone:

- limited resection of the mandible + radiation therapy. Small lesions of the upper gingiva and hard palate:
 - surgical resection + postoperative radiation therapy.

Stage III treatment

Advanced lesions of the lip:

- surgery + radiation therapy (external-beam radiation therapy

with or without brachytherapy, superfractionated);

- chemotherapy (preoperatively, before radiation therapy, as adjuvant therapy after surgery, or as a part of combined modality therapy).

Moderately advanced (late T2, small T3) lesions of the anterior tongue:

- external-beam radiation therapy with or without interstitial implant;
- surgery with postoperative radiation therapy.

Advanced lesions of the buccal mucosa:

- surgical resection + radiation therapy, generally postoperative.

Moderately advanced lesions of the floor of mouth:

- rim resection + neck dissection or partial mandibulectomy with neck dissection + radiation therapy (external-beam + interstitial implant).

Moderately advanced lesions of the lower gingiva:

- combined radiation therapy and radical resection or by radical resection alone.

Advanced lesions of the retromolar trigone:

- surgical composite resection + postoperative radiation therapy-

Moderately advanced lesions of the upper gingiva and of the hard palate:

- radiation therapy alone or a combination of surgery and radiation therapy.

Stage IV treatment

Advanced lesions of the lip:

- surgery + radiation therapy (external-beam radiation therapy with or without brachytherapy, superfractionated).

Advanced lesions of the anterior tongue:

- combined surgery (total glossectomy, sometimes requiring laryngectomy) + combined with postoperative radiation therapy.

Advanced lesions of the buccal mucosa:

- surgical resection + radiation therapy, generally postoperative.

Advanced lesions of the floor of mouth:

- A combination of surgery and radiation therapy (postoperative or preoperative).

Advanced lesions of the lower gingiva:

- poorly controlled by surgery, radiation therapy, or a combination.

Advanced lesions of the retromolar trigone:

- surgical composite resection + postoperative radiation therapy-

Advanced lesions of the upper gingiva and hard palate:

- surgery in combination with radiation therapy. All

stage IV lesions:

- + chemotherapy.

Recurrent treatment

- If radiation therapy was used initially, surgery is the preferred treatment.

- If surgery was used to treat the lesion initially, surgery, radiation therapy, or a combination of these may be considered.
- Although chemotherapy has been shown to induce responses, no increase in survival has been demonstrated.

Diagnostics and treatment algorithm (Fig. 114)

Prognosis

- Small cancers of the retromolar trigone, hard palate, and upper gingiva are highly curable by either radiation therapy or surgery, with survival rates of as much as 100 %.
- Local control rates of as much as 90 % can be achieved with either radiation therapy or surgery in small cancers of the anterior tongue, floor of mouth, and buccal mucosa.
- Moderately advanced lesions of the retromolar trigone without evidence of spread to the cervical lymph nodes are usually curable and have shown local control rates of as much as 90 %; such lesions of the hard palate, upper gingiva, and buccal mucosa have a local control rate of as much as 80 %.
- In the absence of clinical evidence of spread to the cervical lymph nodes, moderately advanced lesions of the floor of mouth and anterior tongue are generally curable, with survival rates of as much as 70 % and 65 %, respectively.
- The overall 5-year survival rate for patients with stage III disease was 30—40 %.

SALIVARY GLAND CANCER

Epidemiology

- These tumors are rare, with an overall incidence in the Western world of approximately 2.5 to 3.0 cases per 100,000 population a year.
- Malignant salivary gland neoplasms account for < 0.5 % of all malignancies and approximately 3 % to 5 % of all head and neck cancers.
- Most patients with malignant salivary gland tumors are in the sixth or seventh decade of life.
- Although exposure to ionizing radiation has been implicated as a cause of salivary gland cancer, the etiology of most salivary gland cancers cannot be determined.
- Occupations associated with an increased risk for salivary gland cancers include rubber products manufacturing, asbestos mining, plumbing, and some types of woodworking.

Affected glands

Major:

- parotid;
- submandibular;
- sublingual.

Minor:

- the oral mucosa, palate, uvula, floor of mouth, posterior tongue, retromolar area and peritonsillar area, pharynx, larynx, and paranasal sinuses;
- minor lesions are most frequently seen in the oral cavity.

Epithelial neoplasms cellular classification

- Pleomorphic adenoma (i.e. mixed tumor).
- Warthin's tumor, also known as papillary cystadenoma lymphomatosum.
- Monomorphic adenomas:
 - basal cell adenoma;
 - canalicular adenoma;
 - oncocytoma;
 - sebaceous adenoma;
 - sebaceous lymphadenoma;
 - myoepithelioma;
 - cystadenoma;
 - ductal papillomas;
 - sialoblastoma.

Low grade

- Acinic cell carcinoma.
- Basal cell adenocarcinoma.
- Clear cell carcinoma.
- Cystadenocarcinoma.
- Epithelial-myoepithelial carcinoma.
- Mucinous adenocarcinoma.
- Polymorphous low-grade adenocarcinoma.

Low grade, intermediate grade, and high grade

- Adenocarcinoma, NOS.
- Mucoepidermoid carcinoma*.
- Squamous cell carcinoma.

Intermediate grade and high grade

- Myoepithelial carcinoma.

High grade

- Anaplastic small cell carcinoma.
- Carcinosarcoma.
- Large cell undifferentiated carcinoma.
- Small cell undifferentiated carcinoma.
- Salivary duct carcinoma.

* *Note:* Some investigators consider mucoepidermoid carcinoma to be of only 2 grades: low grade and high grade.

Cellular classification

- Mucoepidermoid carcinoma.
- Adenoid cystic carcinoma.
- Adenocarcinomas.
 - Acinic cell carcinoma.
 - Polymorphous low-grade adenocarcinoma.
 - Adenocarcinoma, NOS.
 - Rare adenocarcinomas.
 - Basal cell adenocarcinoma.
 - Clear cell carcinoma.
 - Cystadenocarcinoma.
 - Sebaceous adenocarcinoma.
 - Sebaceous lymphadenocarcinoma.
 - Oncocytic carcinoma.
 - Salivary duct carcinoma.
 - Mucinous adenocarcinoma.
 - Malignant mixed tumors.
 - Carcinoma ex pleomorphic adenoma.
 - Carcinosarcoma.
 - Metastasizing mixed tumor.
 - Rare carcinomas.
 - Primary squamous cell carcinoma.
 - Epithelial-myoepithelial carcinoma.
 - Anaplastic small cell carcinoma.
 - Undifferentiated carcinomas.
 - Small cell undifferentiated carcinoma.
 - Large cell undifferentiated carcinoma.
 - Lymphoepithelial carcinoma.
 - Myoepithelial carcinoma.
 - Adenosquamous carcinoma

Symptoms

Most patients are asymptomatic and present with solitary, painless masses.

- The symptoms include:
 - pain,
 - drainage from the ipsilateral ear,

- dysphagia,
- trismus,
- facial paralysis.

Prognostic factors

III The glandes, in which the disease arises.

- Histology.
- Grade (i.e. the degree of malignancy).
- Extent of primary tumor (i.e. the stage).
- Whether the tumor involves the facial nerve, has fixation to the skin or deep structures, or has spread to lymph nodes or distant sites.

Mucoepidermoid carcinomas are graded as low grade, intermediate grade, and high grade. Grading parameters with point values include the following:

- Intracystic component (+2).
- Neural invasion present (+2).
- Necrosis present (+3).
- Mitosis (> 4 per 10 high-power fields (+3)).
- Anaplasia present (+4).

Total point scores are **0 to 4 for low grade, 5 to 6 for intermediate grade, and 7 to 14 for high grade.**

Statistically significant correlation was shown between this point-based grading system and outcome for parotid tumors but not for submandibular tumors. Tumor grade correlated well with prognosis for mucoepidermoid carcinoma of the major salivary glands, excluding submandibular tumors, and minor salivary glands. A modification of this grading system placed more emphasis on features of tumor invasion. Nonetheless, though tumor grade may be useful, stage appears to be a better indicator of prognosis.

Diagnosis

- Gland and lymph nodes ultrasound.
- Biopsy:
 - fine needle aspiration biopsy;
 - core needle biopsy ;
 - localization biopsy;
 - open biopsy.
- Detection of metastatic disease:
 - chest radiography;
 - isotope bone scan;
 - liver ultrasound scan;
 - Brain CT.

TNM staging

Primary tumor

- TX: Primary tumor cannot be assessed.
- TO: No evidence of primary tumor.
- T1: Tumor < 2 cm in the greatest dimension without extraparenchymal extension*.
- T2: Tumor > 2 cm but < 4 cm in the greatest dimension without extraparenchymal extension*.

- T3: Tumor > 4 cm and/or tumor having extraparenchymal extension*.
- T4a: Tumor invades the skin, mandible, ear canal, and/or facial nerve.
- T4b: Tumor invades the skull base and/or pterygoid plates and/or encases carotid artery.

* *Note:* Extraparenchymal extension is a clinical or macroscopic evidence of soft tissues invasion. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.

Regional lymph node involvement

- NX: Regional lymph nodes cannot be assessed.
- NO: No regional lymph node metastases.
- N1: Metastasis in a single ipsilateral lymph node < 3 cm in the greatest dimension.
- N2: Metastasis in a single ipsilateral lymph node > 3 cm but < 6 cm in the greatest dimension, or in multiple ipsilateral lymph nodes < 6 cm in the greatest dimension, or in bilateral or **contralateral** lymph nodes < 6 cm in the greatest dimension.
- N2a: **Metastasis** in a single ipsilateral lymph node > 3 cm but < 6 cm in the greatest dimension.
- N2b: Metastases in multiple ipsilateral lymph nodes < 6 cm in the greatest dimension.
- N2c: Metastasis in bilateral or contralateral lymph nodes < 6 cm in the greatest dimension.
- N3: Metastasis in a lymph node > 6 cm in the greatest dimension.

Metastatic involvement

- MX: Distant metastasis cannot be assessed.
- MO: No distant metastasis.
- M1: Distant metastasis.

- Stage I T1, NO, MO
- Stage II T2, NO, MO
- Stage III T3, N0, M0
 - T1, N1, MO
 - T2, N1, MO
 - T3, N1, M0

Stage IVA

- T4a, NO, MO
- T4a, N1, MO T1, N2, MO T2, N2, MO T3, N2, MO
- T4a, N2, MO

- Stage IVB
 - T4b, any N, MO
 - Any T, N3, M0

- Stage IVC
 - Any T, any N, M1

Treatment

- The minimum therapy for low-grade malignancies of the superficial portion of the parotid gland is superficial parotidectomy.
- For all other lesions, total parotidectomy is often indicated.
- The facial nerve or its branches should be resected if involved by tumor; repair can be done simultaneously.
- Growing evidence suggests that postoperative radiation therapy augments surgical resection, particularly for the high-grade neoplasms, or when margins are close or involved.

- Patients with low-grade tumors that have spread to lymph nodes may be cured with resection of the primary tumor and involved lymph nodes, with or without radiation therapy.

Stage I, II treatment

Low-grade tumors:

- Surgery alone.
- Postoperative radiation therapy should be considered when the resection margins are positive.
- Chemotherapy should be considered in special circumstances, such as when radiation therapy or surgery is refused.

High-grade tumors:

- Localized high-grade salivary gland tumors that are confined to the gland, in which they arise, may be cured by radical surgery alone.
- Postoperative radiation therapy may improve local control and increase survival rates for patients with high-grade tumors, positive surgical margins, or perineural invasion.
- Fast neutron-beam radiation or accelerated hyperfractionated photon beam schedules reportedly are more effective than conventional X-ray therapy in the treatment of inoperable, unresectable, or recurrent malignant salivary gland tumors.

Stage III treatment

Low-grade tumors:

- Surgery alone or with postoperative radiation therapy when indicated.
- Chemotherapy should be considered in special circumstances, when radiation or surgery is refused or when tumors are recurrent or nonresponsive.

High-grade tumors:

- Patients with localized high-grade salivary gland tumors that are confined to the gland, in which they arise, may be cured by radical surgery alone.
- Postoperative radiation therapy may improve local control and increase survival rates for patients with high-grade tumors, positive surgical margins, or perineural invasion.
- Fast neutron-beam radiation or accelerated hyperfractionated photon beam schedules have been reported to be more effective than conventional X-ray therapy in the treatment of inoperable, unresectable, or recurrent malignant salivary gland tumors.

Stage IV treatment

- Standard therapy for patients with tumors that have spread to distant sites is not curative.
- Fast neutron-beam radiation or accelerated hyperfractionated photon beam schedules have been reported to be more effective than conventional X-ray therapy in the treatment of inoperable, unresectable, or recurrent malignant salivary gland tumors.
- Patients with stage IV salivary gland cancer should be considered candidates for clinical trials. Their cancer may be respon-

sive to aggressive combinations of chemotherapy and radiation. Patients with any metastatic lesions could be considered for clinical trials. Chemotherapy using doxorubicin, cisplatin, cyclophosphamide, and fluorouracil as single agents or in various combinations is associated with modest response rates.

Diagnostics and treatment algorithm (Fig. 115)

Prognosis

- The prognosis for any treated cancer patient with progressing or relapsing disease is poor, regardless of the cell type or stage. The disease-free survival was 40 %. Overall survival was 20—25%.
- Disease-free and overall survival for patients with inoperable, unresectable, or recurrent malignant salivary gland tumors is superior in patients treated with fast neutron radiation as compared with conventional X-ray radiation therapy.