CareCore NATIONAL

RADIATION THERAPY MANAGEMENT CRITERIA

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EmblemHealth

Prepared for Emblem Health Provider Network. Clinical criteria for medical necessity review of radiation therapy.

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Dear Provider,

This document provides detailed descriptions of CareCore National's basic criteria for radiation therapy arranged by diagnosis. They have been carefully researched and are continually updated in order to be consistent with the most current evidence-based guidelines and recommendations for the provision of radiation therapy from national and international medical societies and evidence-based medicine research centers. In addition, the criteria are supplemented by information published in peer reviewed literature.

Our health plan clients review the development and application of these criteria. Every CareCore National, LLC health plan client develops a unique list of CPT codes or diagnoses that are part of their radiation therapy utilization management programs. Health Plan medical policy supersedes the CareCore National, LLC criteria when there is conflict with the CareCore criteria and the health plan medical policy. If you are unsure of whether or not a specific health plan has made modifications to these basic criteria in their medical policy for radiation therapy please contact the plan or access the plan's website for additional information.

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Radiation Treatment of Bone Metastases

Conventional external beam radiation therapy utilizing simple 2D planning techniques* is considered medically necessary as palliative treatment for bone metastasis when the patient is experiencing pain, has a high risk of impending fracture or is post-op from repair of a fracture, or has a symptomatic spinal cord compression.

POLICY

I. Fractionation

A. Bedridden more than 50% of the time
   1. Up to 5 Fractions
B. Bedridden less than 50% of the time
   1. Multiple bone metastases
      a. Up to 10 fractions
   2. Solitary metastatic lesion, good prognosis
      a. Up to 14 fractions
   3. Symptomatic spinal cord compression from vertebral metastases
      a. Up to 14 fractions
   4. Other
      a. Up to 10 fractions

II. Technique

A. 2D: Simple planning techniques are appropriate for the majority of patients requiring palliative treatment for bone metastases. One or two gantry angles with unblocked fields can usually produce the appropriate dose distribution. More than one phase (i.e. a cone-down) is rarely appropriate. In rare circumstances where there exists significant extraosseous component or where higher doses are justified, up to 3 gantry angles and use of complex blocking may be justifiable.
B. 3D Conformal and IMRT: Use of conformal radiation therapy techniques including 3-dimensional conformal radiation therapy (3-D CRT) and Intensity Modulated Radiation Therapy (IMRT) are generally considered not medically necessary for the treatment of bone metastasis. 3D conformal therapy will be considered when there is a significant complex extra-osseus component to the target volume. IMRT will be considered only in cases where overlap with previous radiotherapy fields are likely to cause complications.
C. Stereotactic Body Radiosurgery: Stereotactic body radiosurgery (SBRT) is not standard of care [9, 10], and is therefore not considered medically necessary. SBRT will be considered in cases of re-irradiation, or in cases of previous radiotherapy fields being in close proximity. Consideration for the use of SBRT will also be given in cases of radio-resistant tumors

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(sarcoma, melanoma and renal cell carcinoma). Discussion with a CareCore Radiation Oncologist will be required for authorization of cases outside of CareCore standard policy.

Key Clinical Points:

Bone is a common site of metastatic cancer. External Beam Radiation Therapy (EBRT) is the mainstay of treatment for symptomatic bone metastases. Local field radiotherapy is highly effective in relieving pain and preventing fractures and is typically associated with minimal side effects. Eighteen trials assessing fractionation and dose of radiotherapy for painful bone metastases have been published.[1, 2] Randomized trials comparing single fraction of 8 Gy with multiple fraction radiotherapy regimens (20-30 Gy in 5-10 fractions) reveal similar overall response rates. Pain relief is typically achieved 1-4 weeks after treatment and the duration of response is 12-24 weeks. In pooled analysis of patients with bone metastases, approximately one-third of patients will have complete pain relief and an additional one-third of patients will have partial relief of pain, irrespective of the dose-fractionation used.[1] The Radiation Therapy Oncology Group trial 7402 found higher pathologic fracture rate with 40 Gy in 15 fractions compared with 20 Gy in 4 fractions (18% vs. 4%).[3] Radiation Therapy Oncology Group trial 9714 included 452 women with breast cancer and 445 men with prostate cancer.[2] Pain response rates were similar with 8 Gy in one fraction compared with 30 Gy in 10 fractions. Overall response was 66% irrespective of the treatment regimen. The complete pain response was only 17%, without any difference between arms. In patients with one site of painful bone metastasis, the complete pain response rate was 18% with 8 Gy and 25% with 30 Gy (not statistically significant). One-third of patients required no analgesic medication by three months post-treatment. Response was the same irrespective of bisphosphonate use at the time of EBRT. Acute grade 2, 3, and 4 toxicity was seen in 10%, 2.8%, and 0.2%, respectively. More patients experienced toxicity in the higher dose fractionated arm (17% vs.10%). In summary, all trials of radiation fractionation for palliation of bone metastases suggest similar pain relief irrespective of the dose-fractionation schedule.

EBRT alone has most commonly been used for the treatment of spinal cord compression. Corticosteroids are initiated immediately prior to radiation. A total dose of up to 35 Gy in 14 fractions may be appropriate in patients predicted to have more extended life span, although shorter dose schedules including 5 fraction treatment have been employed with similar outcome.[4] A prospective study of 275 consecutive patients with a variety of primary tumors found pain response to radiotherapy in 82% of patients.[5] Three-fourths of patients had preservation of ability to walk or recovery of function. Improvement in sphincter function was noted in 46% of patients with initial deficits. Patients with breast cancer and prostate cancer had better response than those with other solid tumors. Recovery of sensory or motor deficits is related to pretreatment neurologic status. Few patients with paraplegia or incontinence will regain function with radiotherapy. In a study of 70 patients, two-thirds of patients who were ambulatory at the time of radiotherapy remained ambulatory, whereas fewer than one-third of patients who were initially non-ambulatory regained function, and 16% of paraplegic patients regained the ability to walk.[6] Surgery may be appropriate to establish a diagnosis if uncertain, in patients with acceptable performance status where bony retropulsion is likely to be the primary cause of neurologic deficit, in those with rapid deterioration of neurologic function or with high grade cervical cord compression, and can be considered more generally based on the results of a randomized trial comparing surgery and post-operative radiotherapy versus radiotherapy alone. Vertebral body resection and radical decompressive surgery with post-operative radiotherapy was found to be superior to radiotherapy alone in the only randomized trial of spinal cord compression conducted to date.[7] Patients with a single site of cord compression and a minimum three

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month life expectancy were enrolled. The trial was stopped early after 101 patients were enrolled. Patients who received surgery plus EBRT retained the ability to walk significantly longer (126 days vs. 35 days with EBRT alone). In a total of 32 patients who could not walk at the time of enrollment, 56% of those who received surgery and EBRT recovered the ability to walk versus 19% who received EBRT alone. Functional scores, maintenance of continence, and use of steroids and narcotics were all improved in patients undergoing decompressive surgery versus radiotherapy alone. Survival was slightly better in patients undergoing surgery (median 4.2 months vs. 3.3 months, p=0.08). Patients with neurologic deficit and life expectancy of at least 3 months should be considered for surgery based on the results of this phase III study.

The ASTRO Task Force on radiotherapy for bone metastases published its guidelines in 2011 [9]
It clearly states that dosing and target volume have yet to be fully defined for SBRT and that SBRT should be considered investigational. Further, the task force states that SBRT should NOT be the primary treatment of vertebral bone lesions causing spinal cord compression. For recurrent painful lesions, the task force recommends that SBRT should be limited to clinical trials. The summary of the task force is that SBRT "holds theoretical promise in the treatment of new or recurrent spine lesions", and that "its use be limited to highly selected patients and preferably within a prospective trial."

Radiation Fractionation and Technique

Based on available data, the 2008 American College of Radiology Appropriateness Criteria panel recommends single 8 Gy fraction for the palliation of patients with long bone involvement. More than 5 fractions is inappropriate for this group unless there is deemed to be significant risk of fracture or extension into viscera, in which case 30 Gy in 10 fractions is acceptable. Patients with spinal involvement may be considered for treatment using 20 Gy in 5 fractions or 30 Gy in 10 fractions. In cases of symptomatic spinal cord compression or for a solitary bone metastasis and no visceral metastasis, consideration of 35 Gy in 14 fractions may be appropriate, particularly for patients who are deemed to have extended life expectancy, such as those who are chemo-naïve or responsive to systemic therapy or with a long-disease free interval.

However, all patients with poor performance status (bedridden >50% of the time) or predicted life span of less than three months should be treated with single fraction or 5 fraction treatment, to minimize ratio of time on treatment relative to life expectancy.[8]

Simple 2D planning techniques are appropriate for the majority of patients requiring palliative treatment for bone metastasis. According to American College of Radiology Appropriateness Criteria, conformal radiotherapy techniques, including Intensity Modulated Radiation Therapy (IMRT) and protons, are generally inappropriate for the treatment of bone metastases.[8] However; few facilities have traditional simulation machines, and do CT simulation by default. Nonetheless, complex simulation, planning, and treatment charges do not apply in most cases. Therefore one or two gantry angles with unblocked fields can usually produce the appropriate dose distribution. More than one phase (i.e. a cone-down) is rarely appropriate. In rare circumstances where there exists significant extraosseous component or where higher doses are justified, up to 3 gantry angles and use of complex blocking may be justifiable.

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Radiation Treatment of Brain Metastases

In considering optimal treatment for patients with brain metastases, several prognostic factors must be considered. Risk factors for early death include:

1. More than 3 brain metastases
2. Patient not fully ambulatory
3. Diagnosis other than breast cancer
4. Presence of visceral disease
5. Progression of systemic disease after at least one prior chemotherapy regimen for metastatic disease.

POLICY

I. Whole Brain Radiotherapy (WBRT)

A. For patients with most of the risk factors listed above, up to 10 fractions of whole brain radiotherapy is considered appropriate. For patients with better prognosis, up to 15 fractions of WBRT will be considered.WBRT is limited to 2 fields, and 3D conformal planning is considered not medically necessary.

II. Partial Brain Radiotherapy

A. In patients who are fully ambulatory and present with 4 or fewer brain metastases at diagnosis, partial brain radiotherapy as sole phase or a boost is considered medically necessary. Partial brain radiotherapy includes stereotactic radiosurgery (SRS), 3-D conformal treatment, and intensity modulated radiotherapy (IMRT).
   1. SRS is considered medically necessary for up to 4 lesions initially. Further use of SRS will be approved if the patient remains fully ambulatory and systemic disease is under control, and only if the sum of the number of lesions treated at prior episodes plus the number of lesions to be treated at the current episode is not more than 7. For more than 7 lesions, only WBRT is considered medically necessary.
   2. IMRT as the sole treatment of partial brain therapy is considered medically necessary in good prognosis patients, for up to 20 fractions.
   3. When either IMRT or 3D conformal therapy are used for boost treatment, up to 10 fractions are considered medically necessary.
   4. SRS may be considered medically necessary in patients with a good performance status who have previously undergone whole brain irradiation.

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Key Clinical Points:

Whole Brain Radiotherapy (WBRT)

The median survival following the diagnosis of metastatic disease involving the brain is generally four to six months. Many patients develop brain metastases late in the course of their disease when progressive extracranial disease dictates survival. The majority of symptomatic patients will have clinical response with WBRT. The clinical response rate, degree of response, and duration of response depend on the extent of tumor and the severity of initial neurologic deficits. The most common WBRT fractionation is 30 Gy in 10 fractions over two weeks. In two randomized Radiation Therapy Oncology Group (RTOG) trials of over 1800 patients, fractionation schedules of 20 Gy in 1 week, 30 Gy in 2 weeks, 30 Gy in 3 weeks, 40 Gy in 3 weeks, and 40 Gy in 4 weeks were tested[1]. No significant differences between the fractionation regimens were seen. Overall improvement in neurologic function was seen in approximately half of patients and maintained in over three-fourths of these patients. Normal functionality was achieved in one-third of patients that were partly bedridden. Brain metastasis was the cause of death in 40% of patients. Additional randomized trial from the RTOG have shown no significant differences in outcome based on dose-fractionation schemes, including 30 Gy in 2 weeks versus 50 Gy in 4 weeks [2] or versus a hyperfractionated regimen of 54.4 Gy at 1.6 Gy bid[3]. All regimens were associated with response of neurologic symptoms in the majority of patients and a median survival of approximately 4 months. Recursive partitioning analysis of patients treated with a variety of dose-fractionation regimens suggests that factors unrelated to radiotherapy treatment parameters best predict survival: patients with a KPS of at least 70, controlled primary tumor, brain as the only site of metastases, and age less than 65 years were found to have the longest median survival, however even with all of these factors, the median survival was only 7.1 months.[4] Shorter course regimens are appropriate for patients at increased risk of early death, such as those with more than 3 brain metastases, poor performance status, non-breast cancer histology, presence of visceral metastases, and progressive extracranial metastases despite prior chemotherapy. In patients with many of these factors present, treatment regimens longer than 30Gy in 10 fractions is inappropriate, and shorter hypofractionated regimens should be considered. In patients with few of these factors present, consideration could be given to more protracted and aggressive regimens, such as 37.5Gy in 15 fractions.

In patients who have undergone resection, the need for whole brain radiation has been studied. The majority of patients will have further failure in the brain, at both the site of resection and at remote sites in the brain. For example, in a randomized study of 95 patients who underwent MRI-defined complete resection of a solitary brain metastasis, 70% of patients had recurrence in the brain, either at the index lesion or elsewhere. Post-operative WBRT was associated with a three-fourths relative risk reduction in recurrence (absolute risk reduction 18%) and was associated with decreased risk of death from neurologic causes.[5] Therefore, postoperative whole brain radiotherapy is generally recommended for patients who undergo resection of a solitary metastasis and who have controlled extracranial disease. In a patient who has had a solitary metastasis completely resected, there is no established role for partial brain radiotherapy.

Whole brain radiotherapy involves the use of two lateral opposed fields, with or without the use of custom blocking. Often, simple simulation without blocking suffices. Cone-down phase (e.g. boost) is inappropriate in patients undergoing whole brain radiotherapy after complete gross resection of the tumor. Similarly, there

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is no evidence of benefit from partial brain radiotherapy techniques (see below) after gross total resection of brain metastasis.

Partial brain radiotherapy

The survival outcome with WBRT alone for brain metastases is poor and up to half of patients will develop progressive disease with the use of WBRT alone. WBRT is increasingly being supplemented by more aggressive treatment directed at known sites of brain metastases using surgical resection or partial brain radiotherapy techniques such as stereotactic single fraction radiotherapy ("radiosurgery"), stereotactic multi-fraction radiotherapy, 3D Conformal Radiation Therapy (3D-CRT) or Intensity Modulated Radiation Therapy (IMRT).

The value of more aggressive treatment in selected patients is exhibited by two of the three randomized trials of surgical resection of solitary metastasis plus WBRT versus WBRT alone.[6-8] Patchell et al. [6] found improved local control (20% brain failure versus 52%) and median survival (40 weeks versus 15 weeks) with the addition of surgery. In another trial, surgery improved median survival from 6 months to 10 months.[7] A more recently published multicenter randomized trial of 84 patients did not reveal any advantage to surgical resection.[8] This may be due to the selection of patients with worse performance status, more extracranial disease, failure to achieve complete resection in some patients, and crossover of one-fourth of patients receiving WBRT to surgery. Stereotactic radiosurgery offers an alternative means for focal treatment. Radiosurgery is described by the American Society of Therapeutic Radiology and Oncology (ASTRO) as follows: "Stereotactic Radiosurgery (SRS) is a distinct discipline that utilizes externally generated ionizing radiation in certain cases to inactivate or eradicate a defined target(s) in the head or spine without the need to make an incision. The target is defined by high resolution stereotactic imaging. To assure quality of patient care the procedure involves a multidisciplinary team consisting of a neurosurgeon, radiation oncologist, and medical physicist. The adjective "stereotactic" describes a procedure during which a target lesion is localized relative to a fixed three-dimensional reference system, such as a rigid head frame affixed to a patient, fixed bony landmarks, a system of implanted fiducial markers, or other similar system. This type of localization procedure allows physicians to perform image-guided procedures with a high degree of anatomic accuracy and precision. Stereotactic Radiosurgery (SRS) typically is performed in a single session, using a rigidly attached stereotactic guiding device, other immobilization technology and/or a stereotactic image-guidance system, but can be performed in a limited number of sessions, up to a maximum of five. Therapy can be delivered with the Leksell GammaKnife system, which consists of 201 small Cobalt 60 sources all collimated to a single focal point. Another technology allows for linear accelerator-based treatment using a specialized cylindrical collimator placed onto the head of the machine to aim a small radiation beam while the accelerator gantry moves in multiple arcs around a precisely localized target. Fractionated stereotactic radiotherapy can be done using mini-multileaf collimators and less invasive head immobilization and localization procedures. The Cyberknife system is another means to deliver radiosurgery. It utilizes a proprietary image-guidance system and a multi-jointed robotic arm. Radiosurgery is minimally invasive and can be done on an outpatient basis. Patients can return to work or resume normal daily activities the following day.

Selection criteria for radiosurgery are similar to those for surgical resection, i.e. patients with solitary metastases, good performance status, and limited or responsive extracranial disease. In a study of 248 patients with 421 brain lesions from a variety of primary cancers, there was only 11% progression within the radiosurgery volume(s) at a median follow-up of 26 months. Surgery was required for 6% of patients for mass effect or steroid dependency secondary to radiation necrosis.[9] Mehta and colleagues reviewed more

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than 2100 lesions treated with radiosurgery to a median dose of 18 Gy and found 86% of lesions were stable or responded.[10] A retrospective study of 122 patients who were eligible for surgical resection combined 37.5 Gy WBRT followed by a median radiosurgery boost of 17 Gy. An 86% brain tumor control rate was obtained and the median survival was greater than one year, which compares favorably with results of trials of surgical resection and WBRT.[11] RTOG 95-08 randomized patients with 1 to 3 brain metastases to WBRT followed by radiosurgery boost versus WBRT alone (37.5 Gy in 15 fractions). There was improved survival in only the subset of patients with a solitary metastasis (median of 4.9 months in the WBRT arm versus 6.5 months in the WBRT + radiosurgery arm). [12] Therefore, there is likely to be little benefit for radiosurgery in most patients with more than one brain metastasis.

WBRT is generally recommended before or after radiosurgery. In a multi-institutional retrospective study of stereotactic radiosurgery in the treatment of single brain metastasis, of 71 patients who had newly diagnosed brain metastases, the brain control rate at one year was 53% with radiosurgery and WBRT as compared with 18% for radiosurgery alone.[13] However, salvage therapy with WBRT is possible after radiosurgery and survival appears uncompromised with a deferred treatment strategy,[14,15] although it is less appropriate to defer WBRT in patients with more than one brain metastasis or when metachronous lesions appear after an initial course of radiosurgery. Patients with metastasis larger than 3cm are best treated with WBRT as initial treatment as tumor control may be inferior with radiosurgery alone. Patients who respond to WBRT can be considered for radiosurgery. Alternative methods to treat larger solitary brain metastases include partial brain 3D conformal radiotherapy and intensity modulated radiotherapy.

Partial brain radiotherapy with radiosurgery, 3D-CRT, or IMRT should be limited to patients with 4 or fewer active brain metastases who are fully ambulatory and have not had multiple brain lesions previously treated. It is inappropriate to apply partial brain treatment techniques multiple times (e.g. greater than three separate treatment episodes) at the exclusion of whole brain radiotherapy.

ASTRO has published guidelines on radiotherapeutic and surgical management for newly diagnosed brain metastasis/es (2012)[16]There is no convincing evidence of a survival advantage using SRS alone versus WBRT with SRS boost, versus WBRT alone. Randomized trials which have examined the use of radiosurgery, included selected patients with up to 4 brain metastases, while retrospective reports document use of radiosurgery that exceed 4 brain metastases[17,18]. The optimal number of brain lesions that can be safely treated without using WBRT is unknown. While some have postulated that the use of WBRT leads to a more rapid declne in neurocognitive function, the ASTRO guideline states that it remains to be reported whether neurocognitive outcomes differ using SRS versus SRS and WBRT. Of more concern, is that the brain tumor recurrence rate is significantly higher when WBRT is omitted [20], and that there can be a shorter duration to neurocognitive decline attributable to the increased risk of recurrence in patients treated with SRS alone. This increased risk of recurrence in patients receiving SRS alone may be associated with symptomatic recurrence, which may not fully recover despite salvage treatment [19].

If a patient is deemed a candidate for partial brain IMRT as sole treatment, the dose conformality that is achievable generally obviates the need to utilize protracted courses of treatment (i.e. greater than 20 fractions). Additionally, when appropriate, as a boost in conjunction with whole brain radiotherapy, no more than 10 IMRT fractions should be necessary.

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Radiation Treatment of Breast Carcinoma

POLICY

I. Early stage breast cancer

A. For patients who undergo Mastectomy, post-operative chest wall radiotherapy is considered medically necessary in patients with
   1. Multiple positive Axillary lymph nodes
   2. Primary tumor >5cm

B. For patients who undergo Local excision (lumpectomy, breast conservation surgery) adjuvant partial or whole breast radiotherapy is considered medically necessary

Up to 37 fractions is appropriate, including the boost. 3D conformal technique which includes forward planning IMRT (field-in-field, segments) is considered medically necessary. Inverse planned IMRT is not considered medically necessary. Exceptions will be made on case by case basis after discussion with a Carecore radiation oncologist in those unusual clinical situations where inverse planned IMRT dosimetry yields clinically meaningful and significant dosimetric improvement over forward planned dosimetry.

Partial breast radiotherapy is considered medically necessary in those patients with clinical criteria conforming to published guidelines of one of the major societies. Acceptable techniques include EBRT (3D conformal and inverse planned IMRT) and interstitial HDR brachytherapy (Ir-192 or KV energy), up to a total of 10 fractions. Single fraction adjuvant radiotherapy is considered investigational. The accuboost technique is considered investigational.

A boost may be clinically indicated and is considered medically necessary. Boost techniques considered medically necessary include electron and photon energies. For photon energies, up to 3 gantry angles is considered medically necessary A brachytherapy boost is considered not medically necessary.

II. Metastatic breast cancer

A. Symptomatic breast or chest wall disease
   1. Up to 25 fractions if a boost is utilized

Key Clinical Points:

Early stage breast cancer is typically treated with mastectomy with or without radiotherapy to the chest wall, or breast local excision followed by radiotherapy. Indications for post-mastectomy radiotherapy are controversial but include the presence of multiple positive axillary lymph nodes or large primary tumor size (>5cm). Radiotherapy is indicated for most women after local excision of ductal carcinoma in situ or invasive carcinoma. In some women over the age of 70 who have been diagnosed with invasive breast cancer, radiation therapy may be safely omitted especially if they have comorbidities.[1]

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Primary therapy for women with metastatic breast cancer (M1 stage) is systemic therapy. However, if there is symptomatic breast or chest wall disease, a short course of radiotherapy may alleviate symptoms. In most cases, short course hypofractionated treatment (e.g. 10 fractions) is appropriate. It is not appropriate to deliver more than 20 fractions in that setting (or 25 fractions if a boost is included). Evidence is lacking with regard to locoregional radiotherapy for M1 stage disease in the absence of symptomatic locoregional disease. Locoregional radiation therapy may be appropriate for women who initially present with metastatic disease but after surgery and/or chemotherapy are found to have no clinical evidence of disease.

Most women with early stage breast cancer are treated with a 5-7 week course of radiation therapy. Use of simple devices for patient positioning (e.g. angle board) is usually adequate. The 5-7 week course of treatment is based on dose-fractionation considerations that might decrease long term side effects and provide optimal local control of disease. It is inappropriate to use more than 30 fractions (or 37 fractions when a boost is utilized).

Several randomized trials have demonstrated that, for treatment of node negative breast cancer patients, a shorter course of radiation given in just over 3 weeks has been proven to be as effective and was associated with no greater toxicity than five week treatment.[2] Based on this trial and trials in the United Kingdom, an ASTRO task force on whole-breast (WBI) fractionation recently concluded that patients aged 50 years or older, who have disease Stage pT1-2 pN0, do not receive chemotherapy, and are treated with a radiation dose homogeneity within +/-7% in the central axis plane experience equivalent outcomes with either hypofractionated or conventionally-fractionated WBI.[2a] The task force also recommended that the heart should be excluded from the primary treatment fields (when HF-WBI is used) due to lingering uncertainty regarding late effects of HF-WBI on cardiac function. Patients not meeting these criteria were relatively underrepresented in the trials, and few of the trials reported subgroup analyses. Therefore, the task force could not agree for or against the use of HF-WBI in other patients, which nevertheless should not be interpreted as a contraindication to its use. The appropriateness of HF-WBI has also been recognized in the most recent NCCN practice guidelines (version 1.2011; 11/8/2010).

Whole-breast irradiation should give a dose of 45-50 Gy in 1.8-2Gy per fraction, or 42.5 Gy at 2.66 Gy per fraction. All dose schedules are given 5 days per week.

Boost radiotherapy has been shown to improve local control, particularly in younger women. [4] A boost to the tumor bed is recommended in patients at higher risk for local failure (age < 50, positive axillary nodes, lymphovascular invasion, or close margins). Electron beam or photon fields are most commonly used. Typical boost regimens after conventionally-fractionated WBI give total doses of 10-16 Gy at 2Gy/fx. It is appropriate to give up to an additional 4 or 5 fractions for a boost after hypofractionated WBI when a boost if felt to be indicated.

An electron field is the simplest and most available technique used for delivering the boost. Women with deep-seated tumor beds or very large breasts often require treatment with photon boosts, which may consist of two or more fields (e.g., “mini-tangents”, or minitangents plus an anterior oblique).

Interstitial brachytherapy was commonly used for performing the boost during the development of breast-conserving therapy. While the use of brachytherapy in giving the boost is recognized in the NCCN guidelines, it does not improve tumor control compared to external-beam boosts and results in worse

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cosmesis.[4a] Other brachytherapy techniques (such as the MammoSite balloon brachytherapy system) and intraoperative radiotherapy have also been used to perform the boost, but again they have not been shown to be superior to external-beam boosts. Therefore, the use of interstitial or intracavitary brachytherapy or intraoperative radiotherapy in this role is not considered appropriate and will generally not be reimbursed. However, it will be reimbursed for patients who underwent intracavitary brachytherapy or intraoperative radiotherapy under the assumption that these modalities would be used for definitive treatment with APBI but in whom additional information during or after the completion of the procedure was felt to warrant the use of WBI (e.g., the finding of positive excision margins). For chest wall and regional nodal irradiation, the NCCN guidelines state that the appropriate dose is 50 Gy, given as 1.8 - 2.0 Gy fraction size, with or without the addition of a scar boost of 10 Gy given at 2 Gy per fraction, for a total dose of approximately 60 Gy). All dose schedules are given 5 days per week. [3]

The acute side effects of radiation and the cosmetic result can be affected by inhomogeneities of dose within the breast, which, if the simplest methods are applied can be significant given the irregular shape of the breast. Therefore, many methods can be applied to “compensate” for the shape of the breast and improve dose homogeneity by altering the fluence of radiation as it exits the treatment machine. A two dimensional method utilizes tungsten wedges, which are devices placed in the head of the machine to increase the fluence at the base of the breast and decrease the fluence anteriorly, where the tissue is thinner. However, this technique takes into account only the shape of the breast in one plane, and not the entire breast, and has been shown to be associated with more temporary acute skin reactions as compared to more sophisticated 3D techniques.[4]

Three dimensional methods include real-time modulation of the beam to improve the dose distribution, including forward planning 3D conformal radiotherapy with segments to modulate the fluence (also referred to as “step-and-shoot”), forward planning electronic compensation method, and inverse planning Intensity Modulated Radiation Therapy (IMRT). Inverse planning requires dedicated software for IMRT planning in order to calculate and optimize the fluence to the outlined target and spare surrounding organs, which are also outlined. This approach requires trained personnel, patient-specific treatment delivery verification, and specific delivery equipment. Forward planning 3D radiotherapy with segments can be performed with a 3D planning system. The treatment plan consists of several fields with different weights at the same gantry position (called segments). One study compared the dose inhomogeneity within the breast and dose to heart and lung with inverse planned IMRT and 3D segments (typically up to five fields total and two gantry angles) and found no significant differences. [5]

Another large study of 358 patients found no differences in acute toxicity whether the forward planning technique was used as compared with inverse planning (p=0.31). [6]

In addition, forward planning requires less beam-on time, so that scatter to non-target tissues is minimized, which is especially important in young women or smokers, who may have a small increased risk of contralateral breast cancer or lung cancer years after radiotherapy, respectively. An additional advantage of forward planned 3D radiotherapy is that it is widely available. Facilities that perform inverse planning IMRT would have the equipment and personnel to perform forward planned 3D radiotherapy, although the converse is not necessarily true. The forward planning techniques are an extension of 3D conformal therapy. Inverse planning IMRT for breast cancer has no documented advantage over the forward planning step-and-shoot technique and, as mentioned above, results in less beam-on time. Although IMRT is an

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acceptable method of breast irradiation, the IMRT treatment planning and delivery CPT codes will not be reimbursed. In lieu of these codes, the appropriate 3D codes will be reimbursed. An exception will be made when a physician requests the use of multiple-gantry angle IMRT in a patient with left-sided breast cancer in whom forward-planned tangential fields result in excessive dose to the heart. The requesting physician will need to state that plans and dose-volume histograms comparing the IMRT and forward-planned treatment plans have documented a superior result.

Accelerated Partial Breast Irradiation (APBI) is an emerging technique in which the target of the radiation is only a portion of the breast with the greatest likelihood of harboring residual cancer cells after lumpectomy. The technique is called "accelerated" because it is given twice daily for five days, sparing the patient the inconvenience of daily radiation therapy for up to 7 weeks. Treatment is given in a "hypofractionated" fashion, with higher doses per fraction, which can be associated with greater delayed toxicity. This is considered acceptable, because a smaller volume of breast tissue is being treated. However, brisk skin reactions can occur soon after the course of treatment and late skin changes and soft tissue fibrosis could potentially impact the cosmetic result or make the interpretation of future mammography more difficult.

There are several techniques of APBI:

1. Interstitial technique in which multiple needles are placed percutaneously and catheters are threaded into the breast (BRACHYTHERAPY)
2. Intracavitary single catheter balloon catheter, in which a device is placed into the surgical cavity (BRACHYTHERAPY)
3. Intracavitary multiple catheter device – single device with multiple catheter channels inserted into surgical cavity (BRACHYTHERAPY)
4. Multiple non-coplanar field External Beam Radiation Technique (EBRT)
5. Single fraction intraoperative treatment using an External Beam Radiation Technique (EBRT) or an interstitial applicator (BRACHYTHERAPY)

Several single-institution, non-randomized studies using the multicatheter technique have shown low local recurrence rates that are comparable to standard external beam radiation therapy, however, data on newer techniques are still not matured.

There is no consensus on exactly which patients are appropriate candidates for APBI. An ASTRO task force on this subject encouraged patients to participate in clinical trials.[7a] If not eligible for trials, it recommended that patients who may be suitable APBI are women 60 years and older who are not carriers of BRCA 1/2 mutation treated with primary surgery for a unifocal T1N0 ER-positive cancer. Histology should be infiltrating ductal or a favorable ductal subtype, not be associated with EIC or LCIS, and margins should be negative. This was adopted for the most recent NCCN guidelines.[3] However, other groups such as the American Society of Breast Surgeons have promulgated more liberal guidelines in the past (age 45 years old or greater, invasive ductal carcinoma or ductal carcinoma in situ, total tumor size (invasive and DCIS) 3 cm or smaller, negative microscopic excision margins, and pathologically-negative axillary lymph nodes). Further, many experts have contested the correctness of the ASTRO guidelines, with an increasing number of studies showing low failure rates in patients who do not meet these criteria, comparable to that of similar patients treated with WBI (e.g., from the William Beaumont Hospital group[8]). Therefore, it is not clear what standards should be used to deny reimbursement for APBI. Until there is firmer consensus in the

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community, it is reasonable to allow reimbursement for APBI when patients are treated within the guidelines of any of the major professional groups.

The ASTRO and NCCN practice guidelines state that appropriate schemes for APBI are 34 Gy in 10 fractions delivered twice per day with brachytherapy or 38.5 Gy in 10 fractions delivered twice per day. Other fractionation schemes are currently under investigation. It is therefore appropriate at present to reimburse for up to 10 fractions (whether external-beam or brachytherapy) for APBI.

The Axxent electronic brachytherapy (Xoft Inc, Fremont, CA) is a novel way of delivering APBI.[9] Electronic brachytherapy delivers high dose rate (HDR) radiation without radioactive isotopes. In lieu of radioactive isotopes, the electronic brachytherapy system uses a miniature 50 kV X-ray tube, measuring 2.2 mm in diameter as a radiation source.[10] The X-ray source can be turned off and on as necessary. The low energy of the X-ray source allows delivery in minimally shielded settings.[10]

For treatment, the surgeon inserts a balloon applicator into the lumpectomy cavity. The balloon is inflated with saline. The catheter is connected to a robotic controller.[9] At the time of treatment, a protective X-ray shield is placed over the breast. The miniature X-ray source travels into the catheter into the inflated balloon. The X-ray tube is encased in a sheath. Water is pumped through the X-ray sheath to cool the source.[10] After the delivery of the treatment, the X ray source is turned off and withdrawn through the catheter. Treatments are typically delivered in ten fractions, twice daily. The dose-distribution is very similar to that achieved by HDR brachytherapy.

A study by Mehta et al included 44 women treated with Axxent electronic brachytherapy.[11] Eligibility included age > 49, completely resected invasive ductal carcinoma (< 2.0 cm) or ductal carcinoma in situ (< 2.0 cm), lymph node negative, with negative margins of at least 1 mm. The prescribed dose was 3.4 Gy, prescribed to 1 cm beyond the balloon surface. Follow up was 6 months in 43 patients. Four grade 3 toxicities were reported, including pain, blistering and moist desquamation. [11]The study demonstrated that the Axxent system successfully delivered the planned dose of radiation and was well tolerated.

The ASTRO emerging technology committee report on electronic brachytherapy states “that advantages of electronic brachytherapy over existing technologies are as yet unproven in terms of efficacy or patient outcomes. Electronic brachytherapy is currently an unregulated treatment delivery modality for cancer therapy, with minimal clinical data available from small single institution studies, none with any significant follow-up.”[12]

Although the clinical data on this technology is limited, it appears very likely that it will result in results equivalent to those using HDR brachytherapy for APBI, which is reimbursed. Therefore, electronic brachytherapy will be approved for use.

AccuBoost Non Invasive Image Guided Breast Brachytherapy (NIIGBB) (Advanced Radiation Therapy, Inc., Billerica, MA) is an image guided radiation treatment (IGRT) that incorporates a real time image guidance mammography based system to deliver noninvasive brachytherapy.[13] The breast is immobilized using moderate compression. Digital mammography provides localization of the target volume. Custom applicators, ranging from 4-8 cm in diameter, are designed to deliver a highly collimated beam, which are used with an HDR remote after loading system.[13,14] The applicators are mounted on mammography

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paddles, centered on the target to deliver HDR 192 Iridium along two intersecting orthogonal axes sequentially.[14] To use AccuBoost, the tumor bed must be visible on mammogram, the planning target volume must be less than or equal to 8 cm, and the breast must be compressible to a plate separation less than or equal to 7 cm.[13]

Sioshansi et al conducted a study of dose modeling of NIIGBB, compared with electron beam and 3D conformal partial breast radiation.[14] This study modeled the NIIGBB dose distributions as a point source. Dose volume comparisons were evaluated in eight patients and compared to 3DCRT and electron boost simulations. Patient eligibility required a cleared defined target cavity identified on CT, >/= 5mm distance between the posterior aspect of the cavity and the chest wall, and a breast that could be compressed in </= 8 cm. The authors reported that the NIGBB PTVs were significantly less than those of the 3DCRT and electron boost, allowing for more normal tissue sparing. Because NIIGBB directs radiation parallel to the chest wall, there is negligible dose delivered to the chest wall and lung. NIIGBB, compared to electrons and 3DCRT, resulted in lower maximum dose to the skin (60% and 10% respectively), and chest wall/lung (70-90%).[14]

The above study is compelling and warrants further study into NIIGBB. However, there is very little clinical information yet on the use of this approach, which is very different than other techniques used for giving a breast boost or performing APBI. Given the paucity of data regarding the use of NIIGBB, additional research is necessary prior to widespread approval of NIIGBB outside of a clinical trial. NIIGBB will not be reimbursed at this time.

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Radiation Treatment of Craniospinal Tumors – Primary Tumors and Neurologic conditions.

POLICY

Radiation therapy is medically necessary in the following situations

I. Malignant brain tumors - gliomas

Diagnosis must be established with biopsy or resection

A. Post- operative/ post-biopsy
External Beam Radiation Therapy (EBRT) including Intensity Modulated Radiation Therapy (IMRT) and stereotactic radiosurgery (SRS).
   a. Low grade tumors (WHO grade I-II)
      i. Up to 30 Fractions
      ii. 3-D conformal therapy/IMRT
   b. High grade tumors (WHO grade III-IV)
      i. Up to 33 fractions
      ii. 3-D conformal therapy/IMRT

B. Recurrent disease
Case by case consideration for retreatment will be given for those patients with good prognostic factors including an ECOG status of 0, 1, or 2.

C. Investigative- Gliadel wafer/ brachytherapy

II. Primary CNS lymphoma (2D, 3D conformal, IMRT)

A. Younger adults with good performance status and good response to chemotherapy
B. Poor response to chemotherapy
C. Without chemotherapy in patients with a poor performance status, or severely immunocompromised
D. In patients with ocular disease
E. In patients with recurrent disease

III. Benign conditions

The following conditions may be treated with EBRT including 3D conformal, IMRT, and SRS

A. Arteriovenous (AV) malformations (only SRS) and cavernous malformations.
B. Benign brain tumors including pituitary adenomas, acoustic neuromas, schwannomas, craniopharyngiomas, hemangioblastomas, pineocytomas, glomus tumors, and meningiomas. Please note that a maximum of 5 fractions is authorized for stereotactic radiotherapy. For patients prescribed more than 5 fractions, 3D conformal or IMRT technique should be specified as appropriate.

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IV. Neurologic Conditions

Neurologic diseases that are refractory to medical treatment and/ or neurosurgery may be considered for SRS. These diseases include epilepsy, movement disorders (Parkinson's, and essential tremor, familial tremor classifications with major systemic disease) and trigeminal neuralgia. Authorization for this class of diseases will only be granted once all standard treatments have proven to be ineffective. Discussion with a CCN Radiation Oncologist will be required.

V. Primary Spinal Tumors

Inoperable primary spinal tumor with compression or intractable pain may be treated with external beam radiotherapy including 3D conformal, IMRT and SRS.

Key Clinical Points:

Surgical removal is recommended for most types of brain tumors in most locations, and their removal should be as complete as possible within the constraints of preservation of neurologic function. External Beam Radiation Therapy (EBRT) has a major role in the treatment of patients with most tumor types, as evidenced in the EORTC-22845 and MRC-BR04 trials, and can increase the cure rate or prolong disease-free survival[4]. IMRT may yield better dosimetry with sparing of normal brain tissue, especially in dose escalated protocols[2].

High grade gliomas

Since the development of the Radiation Therapy Oncology Group-Recursive Partitioning Analysis (RTOG-RPA) risk classes for high-grade glioma[8], radiation therapy in combination with temozolomide (TMZ) has become standard care[6]. While this combination has improved survival, the prognosis remains poor in the majority of patients. In a phase III randomized study of glioblastoma and anaplastic astrocytoma in the New England Journal of Medicine (NEJM), post-operative EBRT in the elderly statistically significantly improved the median survival compared to observation[7]. Another phase III randomized study of high grade gliomas revealed temozolomide plus EBRT statistically significantly increased the survival rate compared to EBRT alone[6].). For high grade brain tumors (WHO grade III-IV), typically 33 fractions of EBRT are administered post-operatively with up to five coplanar or non-coplanar beams using 3D-CRT or IMRT.

Low grade gliomas

For low grade brain tumors (WHO grade I-II), the role of postoperative radiotherapy (PORT) remains controversial. Cerebral low-grade gliomas (LGG) in adults are mostly composed of astrocytomas, oligodendrogliomas, and mixed oligoastrocytomas. An analysis using data from the European Organization for Research and Treatment of Cancer 22844/22845 studies concluded that several factors portend a poor prognosis: age≥40 years, astrocytoma histology, tumor size ≥6 cm, tumor crossing midline, and preoperative neurologic deficits[1]. PORT may benefit patients with high-risk features. The EORTC trial 22844 did not revealed the presence of radiotherapeutic dose-response for patients with LGG for the two dose levels investigated with this conventional setup[4]. A phase III prospective randomized trial of low- versus high-dose radiation therapy for adults with supratentorial low-grade astrocytoma, oligodendroglioma, and oligoastrocytoma found somewhat lower survival and slightly higher incidence of radiation necrosis in the high-dose RT arm. The most important prognostic factors for survival are histologic subtype, tumor size, and age[3]. For those patients who receive PORT, typically 30 fractions of EBRT are administered with up to

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five coplanar or non-coplanar beams three dimensional conformal radiation therapy (3D-CRT) or Intensity Modulated Radiation Therapy (IMRT).

Recurrent disease

Currently the following options for salvage entered clinical practice: re-resection, re-irradiation (stereotactic radiosurgery, (hypo-) fractionated (stereotactic) radiotherapy, interstitial brachytherapy) or single/poly-chemotherapy schedules including new dose-intensified or alternative treatment protocols employing targeted drugs. A recent review publication concluded that these have only modest efficacy[14]. The relative value of each approach compared to other options is unknown as well as it remains open which sequence of modalities should be chosen. Some patients with recurrent disease may benefit from retreatment with radiotherapy, depending on prognostic factors including grade of tumor, age, and performance status[9,10]. Others factors such as corticosteroid use may be important [11]. A study of several hundred patients retreated for recurrent gliomas at MD Anderson showed that 34 (9%) had complete or partial response, whereas 80 (21%) were alive and progression-free at 6 months (APF6). The median PFS was 10 weeks and median OS was 30 weeks. Histology was a robust prognostic factor across all outcomes. GBM patients had significantly poorer outcomes than AA patients. The APF6 proportion was 15% for GBM and 31% for AA, whereas the median PFS was 9 weeks for GBM and 13 weeks for AA. Results were also significantly poorer for patients with more than two prior surgeries or chemotherapy regimens[12].

Primary CNS lymphoma

The incidence of primary CNS lymphoma dramatically increased in the last several decades, in part related to HIV infection. Primary CNS lymphoma (PCNSL) now accounts for 2-5% of CNS tumors. PCNSL occurs in the brain, leptomeninges, eye and spinal cord. Untreated PCNSL portends a dismal prognosis. Treatment is dependent on age, performance status, extent of disease, and HIV status. Surgery plays little role in the management of PCNSL. Continued investigation is underway to develop the optimal treatment strategy. Recommendations for patients with good performance status include a high dose methotrexate regimen. For younger patients, this is usually followed by radiation (24- 45 Gy in standard fractionation). The timing of radiation is controversial; despite high response rates with a combination of the two modalities, increased neurotoxicity has been observed. Therefore, the recommendation for older (non-immune-suppressed) patients is chemotherapy alone. For patients with poor performance status single modality treatment is used, either radiation therapy or chemotherapy. Radiation is also indicated when there has been an incomplete or limited response to chemotherapy and in the setting of ocular or recurrent disease. For patients with AIDS with low CD4 counts, treatment is usually palliative radiotherapy alone, 30Gy in 10 fractions.

Stereotactic Radiosurgery

Malignant tumors

In 2005, ASTRO published an evidenced based review on the use of stereotactic radiosurgery for malignant glioma[18]. ASTRO concluded that for patients with malignant glioma, there is Level I-III evidence that the use of radiosurgery boost followed by external beam radiotherapy and BCNU does not confer benefit in terms of overall survival, local brain control, or quality of life as compared with external beam radiotherapy and BCNU. The use of radiosurgery boost is associated with increased toxicity. For patients with malignant glioma, there is insufficient evidence regarding the benefits/harms of using radiosurgery at the time progression or recurrence. There is also insufficient evidence regarding the benefits/harms in the use of stereotactic fractionated radiation therapy for patients with newly diagnosed or progressive/recurrent

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malignant glioma. More recent publications have not provided evidence that would change these conclusions. While small, well-defined, unresectable low-grade gliomas are attractive targets for stereotactic irradiation, and fractionated stereotactic irradiation of these targets has the theoretical benefit of increased normal tissue sparing beyond that provided by the physical characteristics of stereotactic radiosurgery, no study has demonstrated its benefit compared to standard techniques. Published results from McGill which includes those of 241 patients treated in nine other institutional series concludes that data regarding the use of SRS is limited and, in their opinion, insufficient to claim a clear therapeutic advantage to SRS in the initial management of low-grade glioma[17] (2006). Several small single institution retrospective studies of higher grade malignancies have been published between 2007 and 2012, and while they claim efficacy, there is no convincing evidence that these are better than standard therapies[13,15,16].

Benign conditions

The success and excellent safety margin of SRS in many other clinical situations has led to exploration of its use in benign tumors and neurologic conditions which are refractory to medical treatment and would otherwise require surgical procedures with significant morbidity and possible mortality. The condition to be treated must be causing severe symptoms or pose a serious threat to function or life expectancy and have an expected benefit of stabilizing or improving the clinical state. Patients with limited life expectancy and/or generally poor performance status (ECOG >2) which are not expected to significantly improve with treatment should not be considered for SRS.

The delivery of SRS may take one to five treatment sessions. By definition the performance of SRS must include:

1. Patient immobilization with or without a frame.
2. Radiographic imaging such as CT, MRI, PET or other radiologic modalities to precisely localize the target area.
3. The use of computerized Image Guidance to insure precise treatment delivery. As per AMA coding guidelines, IGRT is included in the daily treatment delivery code, and may not be billed separately.
4. Dedicated treatment planning and precise calculation with verification of setup and accuracy of all treatment parameters including but not limited to multiple isocenters, arcs, angles, number of beams (size and weight), isodose plans and calculations.
   Accurate simulation and reproducibility of all treatment angles or arcs

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Malignant tumors

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Radiation Treatment of Cervical Cancer

Within the United States in 2008, there were 11,070 new cases of cervical cancer resulting in 3,870 deaths. The prognosis of patients with cervical cancer is markedly affected by the extent of disease at the time of diagnosis.

Typical treatment is as follows:

Stage 0 (Carcinoma in Situ)

Treatment of stage 0 may include the following:

- Loop electrosurgical excision procedure (LEEP)
- Laser surgery
- Conization
- Cryosurgery
- Total hysterectomy for women who cannot or no longer want to have children
- Internal radiation therapy for women who cannot have surgery

Stage IA Cervical Cancer

Treatment of stage IA cervical cancer may include the following:

- Total hysterectomy with or without bilateral salpingo-oophorectomy
- Conization
- Modified radical hysterectomy and removal of lymph nodes
- Internal radiation therapy

Stage IB Cervical Cancer

Treatment of stage IB cervical cancer may include the following:

- A combination of internal radiation therapy and external radiation therapy
- Radical hysterectomy and removal of lymph nodes
- Radical hysterectomy and removal of lymph nodes followed by radiation therapy plus chemotherapy
- Radiation therapy plus chemotherapy

Stage IIA Cervical Cancer

Treatment of stage IIA cervical cancer may include the following:

- A combination of internal radiation therapy and external radiation therapy plus chemotherapy
- Radical hysterectomy and removal of lymph nodes
- Radical hysterectomy and removal of lymph nodes followed by radiation therapy plus chemotherapy

Stage IIB Cervical Cancer

Treatment of stage IIB cervical cancer may include internal and external radiation therapy combined with chemotherapy

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Stage III Cervical Cancer
Treatment of stage III cervical cancer may include internal and external radiation therapy combined with chemotherapy
Stage IVA Cervical Cancer
Treatment of stage IVA cervical cancer may include internal and external radiation therapy combined with chemotherapy

Stage IVB Cervical Cancer
Treatment of stage IVB cervical cancer may include the following:

- Radiation therapy as palliative therapy to relieve symptoms caused by the cancer and improve quality of life
- Chemotherapy
- Clinical trials of new anticancer drugs or drug combinations

POLICY:

I. Curative radiation therapy – definitive or post-operative

A. Brachytherapy Alone
   1. Medically Inoperable
   2. Surgical Refusal
   3. Carcinoma in situ (preinvasive carcinoma)
   4. Invasive Carcinoma diagnosed by microscopy. Microscopic lesions with stromal invasion 3.0 mm or less in depth without lymphatic or vascular space involvement. Visualized lesions are NOT included in this category even with superficial invasion
   5. Palliation to stop hemorrhage in patients with distant disease

B. Pelvic Radiation Alone: EBRT (1, 2,3, 4, 5,); IMRT/IGRT (4,5)
   1. Pre-operative when additional brachytherapy cannot be performed
   2. Definitive treatment when additional brachytherapy cannot be performed and the patient is inoperable
   3. Palliative treatment to stop hemorrhage or for pain relief
   4. As post-operative treatment for positive surgical margins, positive pelvic nodes, close vaginal margins less than 0.5 cm, extensive lymphovascular or capillary involvement.
   5. Treatment of isolated or symptomatic pelvic recurrence

C. Pelvic Radiation and Brachytherapy EBRT (1,2,3,4,5,); IMRT/IGRT (5)
   1. Microscopic lesions with stromal invasion 3.0 mm or less in depth and 7.0 mm or less in horizontal spread with lymphovascular space invasion
   2. All microscopic lesions with stromal invasion more than 3.0 mm
   3. All clinically visible lesions confined to the cervix with or without extension to the parametria, pelvic sidewall (s), lower third of vagina, or causing hydronephrosis or nonfunctioning kidney
   4. Tumor invading the mucosa of the bladder or rectum, and/or extends beyond the true pelvis
   5. As post-operative treatment for positive surgical margins, positive pelvic nodes, close vaginal margins less than 0.5 cm, extensive lymphovascular or capillary involvement.

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Medically necessary Techniques

a. EBRT with brachytherapy. EBRT is typically 3D conformal using up to 4 gantry angles and up to 30 fractions. See below for brachytherapy details
b. EBRT alone in those patients in whom brachytherapy may be contra-indicated
c. IMRT in postoperative treatment

II. Palliative therapy

In the non-curative setting and where symptoms are present, palliative EBRT may be appropriate. In this scenario, treatment is typically delivered with 2D or 3D conformal therapy, up to 4 gantry angles, one phase, and up to 15 fractions.

III. Loco-regional recurrence

If treatment is palliative, see II above. When salvage radiotherapy is attempted, treatment is typically 3D conformal, up to 4 gantry angles, and up to 30 fractions. Two phases may be appropriate, and the use of brachytherapy may be appropriate. IMRT may be considered based on clinical presentation and anatomic location.

Key Clinical Points:

Postoperative External Beam Radiation Therapy (EBRT, IMRT/IGRT)

The use of postoperative radiation treatment in this setting will depend on the type of surgery performed (simple or radical hysterectomy), and the surgical findings. Surgical findings of clinical relevance include the size of the primary tumor, depth of stromal invasion, and presence of lymphovascular invasion. Positive pelvic and /or para-aortic nodes, surgical margins, and involvement of the parametrium are also important. When indicated, postoperative EBRT is typically delivered with 3D conformal radiation therapy, using up to 4 gantry angles, and up to 30 fractions. IMRT with daily IGRT may be used when dose volume histograms show significant benefit as opposed to traditional EBRT. An intracavitary boost may be clinically appropriate in the setting of positive surgical findings. IMRT/IGRT may also be used for pelvic and/or para-aortic radiation treatment when surgical lymph node sampling or dissection is positive for metastatic disease.

Brachytherapy (internal radiation)

Brachytherapy is an important component of the radiation therapy regimen in the curative treatment of cervical cancer. Brachytherapy may be given by both LDR or HDR techniques. Dose recommendations are available in the literature of the American Brachytherapy Society. It is recognized that disease presentations and anatomic deformity may result in less than optimal dosimetry using conventional radiation applicators, and that supplementary interstitial brachytherapy may be required on an individual basis to achieve optimal therapeutic effect.

The type of implant may include tandem and ovoids, tandem alone, ovoids only, interstitial, or vaginal cylinder only. For LDR therapy, up to 2 interstitial or intracavitary applications are considered medically appropriate. For HDR interstitial therapy, when one application is used, up to 5 fractions may be appropriate. When two applications are used, up to 3 fractions may be appropriate. For HDR tandem and ovoids, up to 6 applications may be appropriate. For HDR vaginal cylinder, up to 3 applications are considered appropriate.

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Management of the para-aortic nodes

The treatment of para-aortic nodal regions may be indicated in the following clinical situations:

A. Positive para-aortic lymph nodes on surgical staging if lymph nodes are less than 2cm. and are below L3
B. Positive para-aortic lymph nodes on surgical staging and all macroscopic para- aortic nodes are removed
C. Recurrent disease without evidence of distant metastases
D. Positive pelvic and/or para-aortic lymph nodes on PET, MRI or CT scan. Pathologic confirmation is recommended if technically feasible.

When treatment of the para-aortic nodes is indicated, treatment may be concurrent or sequential. Both regimens are considered medically appropriate. For concurrent treatment, up to 6 gantry angles are approved, and a conedown (additional phase) may be appropriate. For sequential treatment, up to 6 gantry angles, one conedown, and up to 28 additional fractions may be appropriate. If judged clinically necessary by the radiation oncologist and supported by dosimetry analysis, IMRT may be used in lieu of 3-D conformal treatment to reduce doses to critical organs including the kidneys, small bowel, liver and spinal cord.

IMRT and IGRT

The use of Intensity Modulated Radiation Therapy (IMRT) is not routinely appropriate for the definitive treatment of cancer of the cervix as studies have demonstrated difficulty in daily reproducibility and dosimetry. The cervix has been shown to move as much as 2 cm. on a daily basis. Devices for the immobilization of the cervix are considered experimental at this time. Significant and rapid tumor shrinkage seen in cervical cancer can also affect IMRT distributions. Thus, as recommended by the NCCN, certification of IMRT/IGRT treatment involving the intact cervix is restricted to patients participating in IRB protocols. IMRT is considered medically necessary when doses to critical organs can be meaningfully reduced compared to 3D conformal techniques. RTOG 0418 showed that post-operative pelvic IMRT for endometrial cancer is feasible across multiple institutions with use of a detailed protocol and centralized quality assurance. [28] A similar result for cervical cancer is expected from this trial. There is solid evidence that the risk of severe small bowel injury after conventional radiotherapy for post-operative patients with gynecologic cancer is 5-15% [26,27]. Multiple dosimetric studies and smaller clinical studies have demonstrated that dose to the small bowel can be decreased using IMRT, and should impact on the risk of small bowel injury. The major concern at RTOG was the ability of multiple institutions to safely implement IMRT programs for pelvic RT in gyn patients. The conclusion of RTOG 0418 is that this can be done. Additionally, the use of IMRT and IGRT techniques MAY be considered when co-morbid medical conditions and/or surgical history may SIGNIFICANTLY increase risk to critical organs. It is recommended that all IMRT/IGRT treatments be accomplished with photon beams not exceeding 10 MV to reduce integral neutron dose in this highly curable population of patients.

Chemotherapy

Five randomized phase III trials have shown an overall survival advantage for cisplatin-based therapy given concurrently with radiation therapy, while one trial examining this regimen demonstrated no benefit. The patient populations in these studies included women with FIGO stages 1B2 to IVA cervical cancer treated with primary radiation therapy and women with FIGO stages I to IIA disease found to have poor prognostic factors (metastatic disease in pelvic lymph nodes, parametrial disease, or positive surgical margins) at primary surgery, which then go on to receive adjuvant chemoradiation. Although the positive trials vary in terms of the stage of disease, dose of radiation, and schedule of cisplatin and radiation, the trials

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demonstrate significant survival benefit for this combined approach. Based on these results, strong consideration should be given to the incorporation of concurrent cisplatin-based chemotherapy with radiation therapy in women who require radiation therapy for the treatment of cervical cancer.

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Radiation Treatment of Endometrial Cancer

The Radiation Treatment of Endometriod Cancer of the Endometrium

In the United States, there were approximately 40,100 new cases of uterine malignancy in 2008 and approximately 7,470 deaths from this disease. Uterine cancers represent the most common female genital tract malignancy. Endometrioid (tumors resembling the lining of the uterus; adenocarcinomas) are the most prevalent subtype.

Key clinical Points:

The staging definitions used in the creation of the treatment criteria may be found in the 7th Edition of the AJCC Cancer Staging Manual. The treatment options for treatment of cancer of the endometrium are defined by stage of disease, grade of the cancer, completeness of surgical staging and the presence of adverse risk factors. Complete surgical staging is defined as TAHBSO, peritoneal lavage for cytology, dissection of pelvic and para-aortic lymph nodes and careful inspection and palpation of abdominal organs including but not limited to diaphragm, liver, peritoneal surfaces of the abdomen, pelvis, bowel and omentum. Adverse risk factors include advancing age, lymphovascular extension, tumor size, lower uterine involvement classified as cervical glandular involvement (newly classified as Stage I). For cases that are NOT completely surgically staged, radiologic imaging plays an important role in selecting a treatment strategy. Brachytherapy alone or pelvic radiation alone may be considered in Stage IA Grades 1 or 2 with negative imaging. Combined treatment with both modalities may be considered in Stage IA Grade 3 with negative imaging. More extended fields to include the para-aortic nodes, pelvic nodes and brachytherapy may be considered in Stage IA G3, Stage IB or Stage II with negative radiologic and patients with positive pelvic and/or para-aortic lymph nodes on radiologic imaging in non-surgically staged patients with no evidence of other metastatic disease

For all other stages and those with positive radiologic imaging, surgical restaging or pathologic confirmation of more advanced disease is recommended (image directed biopsy). Patients then enter the fully surgically staged treatment recommendations with their newly assigned stage.

Palliation/Recurrence: Either brachytherapy or pelvic radiation alone or combined treatment may be considered based on the clinical presentation. In the non-curative setting and where symptoms are present, palliative EBRT may be appropriate. In this scenario, treatment is typically delivered with 2D or 3D conformal therapy, up to 4 gantry angles, one phase, and up to 15 fractions. When salvage radiotherapy is attempted for recurrence, treatment is typically 3D conformal, up to 4 gantry angles, and up to 35 fractions. Two phases may be appropriate, and the use of brachytherapy may be appropriate. IMRT may be considered based on clinical presentation and anatomic location.

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TREATMENT OPTIONS IN FULLY SURGICALLY STAGED PATIENTS

I. Brachytherapy (Alone)

A. Post-operative:
   1. Stage IA : with adverse risk factors (Grades G1, G2, G3)
   2. Stage IA: without risk factors, (Grades G2, G3)
   3. Stage IB: (Grades G1, G2, G3)
   4. Stage II : (Grade G1)

II. Pelvic Radiation (Alone)

A. Medically Inoperable
B. Post-Operative
   1. Stage IA (G2, G3) with risk factors
   2. Stage IB (G3) without risk factors
   3. Stage IB (G1, G2 G3) with risk factors.
   4. Stage II (G1)
   5. Stage IIIA and Stage IIIB vaginal or parametrial involvement (combination with brachytherapy preferred)
   6. Stage IIIC 1 with positive pelvic nodes and negative para-aortic nodes (G1, G2, G3)

III. Pelvic Radiation and Brachytherapy

A. Post-Operative:
   1. Stage IA with adverse risk factors (G2, G3)
   2. Stage IB without adverse risk factors (G3)
   3. Stage IB with risk factors (G1,G2, G3)
   4. Stage II (G1,G2,G3)
   5. Stage IIIA (G1,G2,G3)
   6. Stage III B
   7. Stage IIIC1 positive pelvic but negative para-aortic nodes

IV. Para-aortic Lymph Node Radiation Treatment With Pelvic Radiation +/- Brachytherapy

A. Stage IIIC 1 (involvement of only pelvic nodes) and IIIC 2 involvement of (para-aortic lymph nodes with or without pelvic nodes) documented at surgery or by image guided biopsy.

V. Tumor Directed Radiation Therapy

A. Tumor Directed RT (Radiation Therapy) has been defined by the NCCN as treatment to sites of known or suspected tumor involvement. Brachytherapy, External radiation to the pelvis and/or para-aortic lymph node regions are included in this definition as are treatments tailored to other specific abdominal or pelvic sites of recurrent, persistent, or presenting cancer. Whole abdominal radiation however, is not included in this definition. The radiation oncologist uses the pathology findings, results of medical imaging, medical history and clinical findings to determine the necessity, techniques and radiation treatment dose regimen.

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B. Stage IVA (tumor invading bladder and/or bowel mucosa) or Stage IV B (distant metastases including inguinal nodes, intra-peritoneal disease, lung, liver or bone metastases) following a debulking surgical procedure with no evidence of gross residual disease or microscopic abdominal disease.
C. Recurrence
D. Palliation including primary and/or metastatic disease sites

TREATMENT DISCUSSION:

A. Brachytherapy: Current guidelines for the use of brachytherapy in the treatment of endometrial cancer with HDR from the American Brachytherapy society may be found in the International Journal of Radiation Oncology Biology & Physics, 2000 Oct 1; 48 (3):779-90. Additional information is available from the American Brachytherapy Society survey in the International Journal of Radiation Oncology ,Biology & Physics, 2005 Dec1;63(5):1502-7
   Consistent with published guidelines including NCCN, appropriate medically necessary treatments are:
   1. Pre-operative Stage II with gross disease: External beam radiotherapy and intrauterine brachytherapy to a total dose of 75 to 80 GY low dose rate equivalent.
   2. Post-operative: Following the performance of a hysterectomy, brachytherapy using a vaginal cylinder is generally limited to the upper vagina with the dose prescribed at the vaginal surface or to a depth of 0.5cm. HDR vaginal cylinder regimens of 5 to 6 GY for 2 fractions to the vaginal mucosa are common in conjunction with external beam treatment. As definitive treatment alone without EBRT, HDR regimens using a vaginal cylinder include 7GY x 3 to a depth of 0.5cm from the vaginal surface or 6GY x 5 to the vaginal surface.
B. External beam doses to the pelvis and tumor volume for microscopic disease range from 45 to 50 GY usually in 180 cgy daily fractions. CT planned 3-Dimensional techniques are generally used. For treatment of the post-operative pelvis with planned external beam boosts to positive lymph nodes or positive surgical margins, IMRT may be considered medically necessary to reduce doses to critical organs. IMRT may also be considered for post-operative pelvic radiation as part of a sequential or concurrent treatment plan incorporating the para-aortic lymph node treatment.
C. External beam doses to the para-aortic region: When treatment of the para-aortic nodes is indicated, treatment may be concurrent or sequential. Both regimens are considered medically appropriate. For concurrent treatment, up to 6 gantry angles are approved, and a conedown (additional phase) may be appropriate. For sequential treatment, up to 6 gantry angles, one conedown, and up to 28 additional fractions may be appropriate. If judged clinically necessary by the radiation oncologist and supported by dosimetry analysis, IMRT may be used in lieu of 3-D conformal treatment to reduce doses to critical organs including the kidneys, small bowel, liver and spinal cord. IMRT may also be considered for post-operative para-aortic radiation as part of a sequential or concurrent treatment plan in which IMRT is being administered to the post-operative pelvis with planned external beam boosts to positive lymph nodes or positive surgical margins.
D. IMRT and IGRT. The use of Intensity Modulated Radiation Therapy (IMRT) is not routinely appropriate for the treatment of cancer of the uterus as studies have demonstrated difficulty in

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daily reproducibility and dosimetry. Thus, as recommended by the NCCN, certification of IMRT/IGRT treatment involving the intact uterus is restricted to patients participating in IRB protocols. . IMRT is considered medically necessary in the post-operative setting when doses to critical organs can be meaningfully reduced compared to 3D conformal techniques. RTOG 0418 showed that post-operative pelvic IMRT for endometrial cancer is feasible across multiple institutions with use of a detailed protocol and centralized quality assurance. [17] A similar result for cervical cancer is expected from this trial. There is solid evidence that the risk of severe small bowel injury after conventional radiotherapy for post-operative patients with gynecologic cancer is 5-15% [15,16]. Multiple dosimetric studies and smaller clinical studies have demonstrated that dose to the small bowel can be decreased using IMRT, and should impact on the risk of small bowel injury. The major concern at RTOG was the ability of multiple institutions to safely implement IMRT programs for pelvic RT in gyn patients. The conclusion of RTOG 0418 is that this can be done. It is recommended that all IMRT/IGRT treatments be accomplished with photon beams not exceeding 10 MV to reduce integral neutron dose in this highly curable population of patients.Chemotherapy: The use of chemotherapy and radiation treatment in the management of endometrial cancer either concurrently or sequentially remains for the most part the object of clinical study and investigation. Consideration to combined modality treatment may be considered in patients with high risk of recurrence, recurrent or metastatic disease. Current disease presentations considered for chemotherapy and radiation include but are not limited to are Stage IB and Stage II Grade 3 and Stages III A,B,C; Stages IVA and IB in fully surgically staged patients. In those who are not completely surgically staged consideration may be given for the use of chemotherapy and chemotherapy in patients with negative imaging studies in Stage IA G3 and all grades in Stage IB, and Stage II. Those with positive imaging studies are treated according to further surgical and/or biopsy results.

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Radiation Treatment of Gastric Adenocarcinoma

Radiation Therapy is indicated when a tissue diagnosis of gastric adenocarcinoma has been made and the patient is a surgical candidate.

A. Surgical resection planned or performed [1 or 2]
   1. Neoadjuvant treatment (before surgery)
   2. Adjuvant treatment (after surgery)
      a. Tumor stage T2, T3 or T4
      b. Lymph nodes positive for tumor at surgery and no residual disease
      c. Microscopic residual disease with positive surgical margins
      d. Select patients with high risk features of poor differentiation, lymphovascular Invasion, neural invasion, age less than 50

B. Radiation treatment plan
   1. Fields- up to 4
   2. Fractions- up to 28 with doses of 45 to 50.4 Gy.
   3. Customized blocking
   4. CT simulation
   5. 3-D conformal therapy
   6. IMRT may be indicated when dose to the small bowel is of concern.

C. Local recurrence or palliation

   For symptomatic patients with local recurrence not amenable to surgical salvage, or in the palliative setting, a brief course of radiotherapy using 2D or 3D technique, up to 4 fields, and up to 15 fractions may be indicated

Policy:

CCN supports the use of adjuvant chemoradiotherapy in resectable advanced gastric cancer as medically necessary. Advanced is defined as T2, T3 or T4 and /or node positive tumors. 3D conformal radiotherapy is deemed appropriate, but IMRT will be considered in those cases in which clinically meaningful reduction in doses to critical organs can only be achieved with IMRT.

Key Clinical Points:

The intergroup 0116 Gastric Surgical Adjuvant Trial randomized high risk (T3,4 and/or node positive), completely resected gastric or gastroesophageal adenocarcinomas to receive either observation alone or radiochemotherapy. [1] Radiochemotherapy produced significant improvements in relapse-free and overall survival. Radiotherapy was given to a dose of 45 Gy in 25 fractions, usually via AP-PA fields. Thirty five percent of initially submitted radiotherapy plans in the Gastric Surgical Adjuvant Trial had major or minor treatment errors at initial review, demonstrating the difficulty many clinicians had in implementing the complex radiotherapy field.[1,2] Toxicity was significant, with 49% of patients experiencing NCI-Common Toxicity Criteria Grade 3 or worse.

The Medical Research Council Adjuvant Gastric Infusional Chemotherapy Trial (MAGIC) proved that patients with operable adenocarcinoma of the stomach derived benefits in terms of decreased tumor size

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and stage, as well as improved progression-free survival and overall survival from a perioperative regimen of chemotherapy (epirubicin, cisplatin and fluorouracil).[3] The use of RT was omitted.
In terms of historical progression of treatment planning techniques, after the intergroup 0116 trial, which used AP-PA field arrangement, in 2007 Soyfer et al published data concluding that non coplanar 3D conformal approach yielded better results than AP-PA plans.[4] In 2008 this same group compared IMRT to 3D conformal techniques for adjuvant management of gastric cancer and concluded that IMRT confers only marginal benefit and should be used "only in the small subset of patients with risk factors for kidney disease or those with preexisting nephropathy." [5] In 2010, the group at Stanford published on sequential groups of patients treated in the adjuvant setting, initially 3D conformal (26 patients), and after 2002 with IMRT (33 patients).[6] The 2-year OS for the 3D CRT and IMRT groups was 51% and 65%, respectively (*P* = .5). The 2-year DFS for the 3D CRT and IMRT groups was 60% and 54%, respectively (*P* = .8). The 2-year local control rate for the 3D CRT and IMRT groups was 83% and 81%, respectively (*P* = .9). The Stanford group interpreted this data to show that IMRT could be delivered effectively without compromising outcome. In terms of toxicity, three patients required a treatment break of a median duration of 7 days due to toxicity in the 3D CRT group (range, 4-10 days), whereas no patient in the IMRT group required a treatment break. Grade 2 or higher acute GI toxicity was noted in 61.5% and 61.2% of patients in the 3D CRT and IMRT groups, respectively. Late toxicity : Among the 3D CRT patients, 1 patient died of small bowel perforation requiring surgical intervention (grade 5). Grade 3 late toxicity was experienced by 3 patients who developed small bowel obstruction. Two patients developed grade 2 late toxicity (jaundice and esophagitis). In the IMRT group, grade 3 late toxicity was experienced by 1 patient who had a stricture requiring surgery. Grade 2 late toxicity was experienced by 3 patients: 1 with gastritis, 1 with esophagitis, and 1 with an ulcer. The conclusion of this paper was "although locoregional control is good with adjuvant chemoradiotherapy, overall outcomes for gastric cancer remain poor. Improvements in both local and systemic therapy are required. Adjuvant chemoradiotherapy was well tolerated with either 3D CRT or IMRT, with similar acute and late toxicities reported. Despite higher doses used, IMRT provides sparing to the liver and possibly the kidneys." A study from China documents successful implementation of IMRT for postoperative gastric cancer at a single institution.[9] MD Anderson has used IMRT in the preoperative setting for gastric cancer.[10] A recent publication from Memorial Sloan Kettering documents that a lower dose to the heart and coronary arteries can be achieved with IMRT compared to 3D conformal technique, in the treatment of distal esophageal cancer [7]. It is not clear what the clinical significance of this is.
NCCN guideline version 2.2011 describes the use of either AP-PA or 4 field 3D conformal as appropriate, with a dose of 45 – 50.4 Gy. The guideline states that IMRT may be appropriate in selected cases to reduce dose to the normal structures including heart, lung, kidneys, and liver.
NCCN guideline version 1.2012 states that surgery alone is an insufficient treatment for most patients. Based on the results of the MAGIC trial, perioperative chemotherapy or chemoradiation may be considered for patients with more advanced disease (T2 or higher, and N). Based on the results of the INT -0116 trial, postoperative chemoradiation is recommended for selected patients.

Summary:

While the intergroup 0116 trial documented the benefit of adjuvant chemoradiotherapy, and the MAGIC trial documented the benefit of chemotherapy in the perioperative setting, there is currently an ongoing European trial (CRITIC) to specifically study the contribution radiotherapy in the adjuvant setting in patients with resectable gastric cancer[8]. Pending the outcome of this trial, CCN supports the use of adjuvant radiotherapy in resectable high risk gastric cancer as medically necessary. 3D conformal radiotherapy is

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deemed appropriate, but IMRT will be considered in those cases in which clinically meaningful reduction in doses to critical organs can only be achieved with IMRT.

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Radiation Treatment of Head and Neck Cancer

Description:

Based upon established criteria, assessment of peer-reviewed literature, and consensus present in established guidelines (ACR/ASTRO, NCCN), radiation therapy is considered an integral component in the multidisciplinary management of malignancies of the head and neck region. Primary anatomic sites included in this category include paranasal sinuses (ethmoid and maxillary), salivary glands, the lip, oral cavity, oropharynx, hypopharynx, glottic larynx, supraglottic larynx, nasopharynx, and occult/unknown head and neck primary sites. The preponderance of literature addresses tumors of epithelial origin. Non-epithelial malignancies of the head and neck region (e.g. tumors arising in bone, cartilage, soft tissues, and lymphomas) are not covered by this policy.

Utilization of radiation therapy should be preceded by patient workup and staging, and planned in conjunction with the appropriate members of a multi-disciplinary team that also includes: diagnostic imaging, pathology, medical oncology; otorhinological, oral, plastic and reconstructive, neuro- and ophthalmologic surgeons; psychiatry; addiction services; audiology and speech therapy; rehabilitation and nutritional medicine; pain management, dentists, prosthodontists, xerostomia management, smoking and alcohol cessation, tracheostomy and wound management, social workers and case management. Participation in a national clinical trial is encouraged.

Initial management may require surgery, chemotherapy, and radiation therapy in various combinations and sequences.

Work-up Policy:

Work-up of patients with epithelial malignancies of the head and neck region varies by site and extent of disease to include:

- Physical examination, including (when applicable) endoscopic assessment.
- Imaging appropriate to the primary site and clinical extent of disease. This may require CT with contrast, MRI, PET-CT, panorex, speech and swallowing studies.
- Establishing the stage of disease, its potential for resection, and the patient's anticipated ability to withstand radiation therapy and chemotherapy are all part of the initial evaluation.
- Biopsy
- Laboratory testing, including HPV.

Radiation Treatment Schedules:

Radiation Therapy treatment schedules published in peer-reviewed consensus documents such as NCCN Practice Guidelines in Oncology include the following regimens that encompass a broad range of dose that must be customized to an individual patient's circumstance. These schedules are applicable for specific combinations of tumor primary site, extent of primary and nodal disease, pre- post- or non-operative status, inclusion of brachytherapy, the use of concurrent chemotherapy, and co-morbidities/general health of the patient:

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Primary Site, Definitive:
- Conventional schedule: 50-74 Gy at 2.0 Gy/daily fraction, +/- brachytherapy
- Accelerated fractionation schedule: 66 - 74 Gy in 30 fractions, 6 fractions per week
- concomitant boost accelerated schedule: 72 Gy in six weeks, with twice-daily treatments on each of the final 12 treatment days
- Hyperfractionation schedule: 81.6 Gy/1.2 Gy twice daily (68 fractions)
- 63 - 66 Gy at 2.25 - 2.0 Gy/daily fraction

Primary Site, Post-Operative:
- >= 60 Gy at 2.0 Gy/daily fraction

Gross Adenopathy:
- 66-74 Gy at 2.0 Gy/daily fraction

Uninvolved Nodal Stations at Risk:
- 44-64 Gy at 1.6 - 2.0 Gy/daily fraction

Post-operative Nodal Sites:
- Involved nodes: 60 - 66 Gy at 2.0 Gy/daily fraction
- Uninvolved nodes at risk: 44 - 64 Gy at 1.6 - 2.0 Gy/daily fraction

POLICY

Radiation Therapy, External Beam Techniques:

3D-conformal, Intensity Modulated (IMRT), and Image-guided (IGRT) techniques are considered medically necessary when the extent of disease allows preferential sparing of organs not needing radiation without compromising the dose delivered to tumor. In certain situations in which the extent of disease precludes better sparing of organs at risk by IMRT, an IMRT technique may not be medically necessary. In certain situations of limited disease, IMRT is not medically necessary.

Adaptive therapy is considered medically necessary, with re-planning upon significant alteration of tumor status or neck contour due to weight change.

The use of photon beam and electron beam radiation therapy is medically necessary.

The use of neutron beam therapy is regarded as medically necessary in select cases of salivary gland tumors.

Pre-operative radiation therapy is medically necessary in select cases, and may be given in up to 35 fractions in 3 phases, and may use 2D, 3D conformal, or Intensity Modulated, Image-guided technique.

Definitive radiation therapy is medically necessary for selected T1-2, N0 cases as monotherapy and may employ up to 42 fractions in a maximum of 2 phases. Depending on the simplicity or complexity of the case, a 2D, 3D conformal, or Intensity Modulated, Image-guided approach may be necessary.

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Definitive radiation therapy as monotherapy is medically necessary for selected T1N1 and T2N0-1 cases. Radiation may be given utilizing any of several schedules including conventional daily fractionation, concomitant boost accelerated fractionation, and hyperfractionation (twice-daily radiation). Up to sixty-eight (68) fractions may be medically necessary, in 2 phases.

Definitive concurrent chemoradiation is medically necessary in unresected T2-4a, N0-3 cases utilizing up to 42 fractions with conventional schedule. 3D-conformal and Intensity Modulated, Image-guided techniques are considered medically necessary, in up to 4 phases. Concurrent chemotherapy carries a high toxicity burden and requires substantial supportive care and the expertise of an experienced multidisciplinary team.

Post-operative radiation therapy is medically necessary for cases which have any of the following high risk factors:

- pT3 or pT4 primary tumors
- N2 or N3 nodal disease
- Positive nodes in levels IV or V
- Perineural invasion
- Vascular tumor embolism

Thirty-five fractions are medically necessary. 3D-conformal and Intensity Modulated, Image-guided techniques are considered medically necessary, in up to 3 phases.

Chemotherapy may be added concurrently with post-operative radiation and is medically necessary in cases with positive margins or extracapsular nodal spread. Concurrent chemotherapy also may be considered in cases with the other high risk factors mentioned above, in which up to 40 fractions in two phases are medically necessary. Concurrent chemotherapy carries a high toxicity burden and requires substantial supportive care and the expertise of an experienced multidisciplinary team.

Radiation Therapy, brachytherapy:

Low dose rate or high dose rate brachytherapy is medically necessary in select cases of epithelial tumors of the head and neck region. In appropriate early cases it is medically necessary as monotherapy. In non-early cases it may be substituted for one external beam phase.

Brachytherapy for head and neck malignancies should be performed only by those radiation oncologists specifically trained in its use.

Radiation Therapy, palliative:

In previously un-irradiated patients with symptomatic local disease, external beam radiation is indicated for symptom control. Up to 15 fractions are medically necessary, in one phase.

Re-treatment for salvage after prior radiation:

Re-irradiation may be indicated in cases of recurrent or persistent disease, or for in-field new primary tumors, in cases in which there are no known distant metastases. Reirradiation carries increased risk. Enrolment in a clinical trial is preferred. SBRT may be medically necessary for retreatment in patients who have no evidence of metastatic disease.

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Radiation Treatment for Hodgkin's Lymphoma

Description:

Based upon established criteria, assessment of peer-reviewed literature, and consensus present in established guidelines (ACR/ASTRO, NCCN), radiation therapy is considered an integral component in the multidisciplinary management of Hodgkin's lymphoma (HD). Proper management of the disease requires the cooperation of a complex multi-disciplinary team that includes experts in diagnostic imaging, pathology, radiation oncology and medical oncology. HD treatment is based on initial stage of disease as well as the medical condition of the patient, and treatment is dynamically modified based on the speed and extent of response to initial therapy. At diagnosis, areas of involvement may be supra-diaphragmatic only, sub-diaphragmatic only, or a combination of the two in the more advanced stages, and the stage determines decisions made about the proper extent of radiation. The varied pathologic subtypes, for the most part at present, do not materially affect the dose or field decisions to be made in this disease.
Treatment decisions are preceded by patient workup and staging, and planned in conjunction with the appropriate members of the multi-disciplinary team. Participation in a national clinical trial is encouraged. Initial management will usually require chemotherapy (in a variety of different acceptable regimens), followed by assessment of response leading to an appropriate choice of doses and fields of radiation therapy. Chemotherapy alone may be appropriate for early stage non-bulky disease, with radiation therapy reserved for relapse.

Workup Policy:

Work-up of patients with HD includes:

- Physical examination
- Imaging appropriate to the clinical extent of disease. This may require CT with contrast, MRI, PET-CT, gallium scans and bone scans.
- Bone marrow assessment in the more advanced stages
- Ancillary pulmonary and cardiac function tests in preparation for potential chemotherapy
- Fertility and pregnancy assessment in the pre-menopausal female
- Biopsy
- Laboratory testing, including HIV

Radiation Treatment Schedules

Radiation Therapy treatment schedules published in peer-reviewed consensus documents such as NCCN Practice Guidelines in Oncology include regimens that encompass a range of doses and fields that may be influenced by the initial stage, bulk of the disease at each site, the choice of chemotherapy regimens, and the response to initial chemotherapy. Using current combined modality approaches, the fields covered are usually confined to the initial areas of documented involvement.

Stage I and II disease – treatment is given after initial chemotherapy to the original extent of disease, omitting sites that had no clear involvement in an effort to minimize toxicity, to doses that range from 20-36

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Gy. These are generally encompassable in a single site setup, requiring the use of 2D or 3D techniques, with image guidance.

Stage III and IV disease – radiation, if given, is response driven and dependent on original bulk of disease. To sites of original bulky disease, doses of 30-40 Gy may be appropriate, even if there is a CR to chemotherapy, and is routinely considered if there is less than a CR.

Relapsed patients – In patients who relapse after chemotherapy alone for early stage disease, salvage chemotherapy and radiation therapy may be chosen. In select cases at diagnosis, definitive radiation may be appropriate, with the use of sub-total lymphoid irradiation to doses of 25-36 Gy.

POLICY

Radiation Therapy, external beam techniques:

2D and 3D-conformal techniques are considered medically necessary for the treatment of HD. Respiratory gating techniques and image guidance techniques may be appropriate to minimize the amount of critical tissue (such as lung) that is exposed to the full doses of radiation. Only rarely can a justification be made for the use of more advanced IMRT techniques when the extent of disease allows preferential sparing of organs not needing radiation without compromising the dose delivered to tumor. In most situations of limited disease, due to the relatively low doses required, IMRT is not medically necessary.
The use of photon beam and electron beam radiation therapy is medically necessary.

Definitive radiation therapy as sole therapy is medically necessary for selected cases of stage I-IIA lymphocyte predominant Hodgkin's lymphoma. These cases may require doses up to 36 Gy, directed at a single site in a single phase, using 2D or 3D techniques with possible image guidance. Rare cases of patients unable to receive effective chemotherapy may be treated with definitive radiation to doses of 30-36 Gy. Depending on the extent of the disease, a 2D or 3D conformal approach, with Image-guidance, will be necessary. In these cases, treatment of up to three sites may be required, in up to 2 phases per site, using 2D or 3D techniques with image guidance.

Adjuvant radiation after chemotherapy is medically necessary in most cases of patients with stage I-IIB disease, to areas of initial involvement, to doses from 20- 40 Gy, up to 23 fractions with conventional schedule. 2D or 3D-conformal techniques, with image guidance, are considered medically necessary, directed at a single field in up to 2 phases. Adjuvant radiation after chemotherapy is medically necessary in some cases of patients with stage III-IV disease, to areas of initial bulky involvement or to areas of less than a CR, to doses from 20- 40 Gy, up to 23 fractions with conventional schedule. 2D or 3D-conformal techniques, with image guidance, are considered medically necessary, directed at up to 4 separate sites, in up to 2 phases apiece. Concurrent chemotherapy carries a high toxicity burden and requires substantial supportive care and the expertise of an experienced multidisciplinary team.

Salvage radiation therapy is medically necessary after chemotherapy to areas of relapsed bulky involvement, to doses from 20- 40 Gy, up to 23 fractions with conventional schedule. 2D or 3D-conformal techniques, with image guidance, are considered medically necessary, directed at up to 4 separate sites, in up to 2 phases apiece. Salvage radiation therapy may be medically necessary in cases of relapse after solo chemotherapy for initial stage I/IIA disease. Such patients may be treated with definitive radiation to doses of 30-36 Gy, in up to 23 fractions. Depending on the extent of the disease, a 2D or 3D conformal

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approach, with Image-guidance, will be necessary. In these cases, treatment of up to three sites may be required, in up to 2 phases per site, using 2D or 3D techniques with image guidance.

Radiation Therapy, palliative:

In patients with advanced or recurrent disease who are felt not to be curative, with symptomatic local disease, external beam radiation is indicated for symptom control. Up to 10 fractions are medically necessary, in one phase, using 2D or 3D techniques.

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Radiation Treatment for Non-Hodgkin's Lymphoma

Description:

Based upon established criteria, assessment of peer-reviewed literature, and consensus present in established guidelines (ACR/ASTRO, NCCN), radiation therapy is considered an integral component in the multidisciplinary management of Non-Hodgkin's lymphoma (NHL). Proper management of the disease requires the cooperation of a complex multi-disciplinary team that includes experts in diagnostic imaging, pathology, radiation oncology and medical oncology. NHL treatment is based on the pathologic subtype of the disease, initial stage of disease as well as the medical condition of the patient. Pathology and stage have a critical role in the planning process.

Treatment decisions are preceded by patient workup and staging, and planned in conjunction with the appropriate members of the multi-disciplinary team. Participation in a national clinical trial is encouraged. Initial management requires chemotherapy as the cornerstone of therapy (in a variety of different acceptable regimens), followed by assessment of response leading to an appropriate choice of doses and fields of radiation therapy that may improve the chance of control.

Workup Policy:

Work-up of patients with NHL includes:

- Physical examination.
- Imaging appropriate to the clinical extent of disease. This may require CT with contrast, MRI, PET-CT, gallium scans and bone scans.
- Bone marrow assessment in the more advanced stages.
- Ancillary pulmonary and cardiac function tests in preparation for potential chemotherapy.
- Biopsy.
- Laboratory testing, including HIV status.

Radiation Treatment Schedules

Radiation Therapy treatment schedules published in peer-reviewed consensus documents such as NCCN Practice Guidelines in Oncology include regimens that encompass a relatively limited range of doses and fields that may be influenced by the histology, initial stage, bulk of the disease at each site, the choice of chemotherapy regimens, and the response to initial chemotherapy. Using current combined modality approaches, the fields covered are usually confined to the initial areas of documented involvement.

Recommendations are histology specific. For instance, patients with CLL (chronic lymphocytic leukemia) will not require radiation routinely.

Follicular low grade lymphoma, stage I or II – radiation alone may be considered adequate therapy, or radiation treatment may be given after initial chemotherapy to the original extent of disease, omitting sites that had no clear involvement in an effort to minimize toxicity, to doses that range from 20-36 Gy. These are generally encompassable in a single site setup, requiring the use of 2D or 3D techniques, with image guidance. Radioimmunotherapy may be appropriate.

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Follicular lymphoma, stage III/IV – systemic chemotherapy is the standard of care. Radiation may be considered for patients with a sub-optimal response to therapy.
Transformed lymphoma – those patient with originally follicular lymphoma that have transformed to a more malignant subtype – systemic chemotherapy is the mainstay of therapy, and radiation may be considered as an adjunct for locally uncontrolled disease. Radioimmunotherapy may be appropriate.

MALT-lymphoma (Gastric or non-gastric) – radiation may be appropriate as curative therapy, to doses of 36 Gy.

Extranodal NK/T-cell lymphoma, nasal lymphoma – definitive RT to a dose of 54 GY may be appropriate therapy.

For the following histologies, radiation may be appropriate as consolidative therapy after initial chemotherapy, to a dose of 36 Gy to the original extent of disease:

- Mantle cell lymphoma
- Diffuse large cell B-cell lymphoma (DLBCL)
- Burkitt's Lymphoma
- Lymphoblastic lymphoma
- Primary cutaneous B-cell lymphoma
- Peripheral T-cell lymphoma

POLICY

Radiation Therapy, external beam techniques:

2D and 3D-conformal techniques are considered medically necessary for the treatment of NHL. Respiratory gating techniques and image guidance techniques may be appropriate to minimize the amount of critical tissue (such as lung) that is exposed to the full doses of radiation. Only rarely can a justification be made for the use of more advanced IMRT techniques, such as high neck involvement where the extent of disease allows preferential sparing of organs (salivary glands) not needing radiation without compromising the dose delivered to tumor. In most situations of limited disease, due to the relatively low doses required, IMRT is not medically necessary. The use of photon beam and electron beam radiation therapy is medically necessary.

Definitive radiation therapy as sole therapy is medically necessary for selected cases of stage I-IIA low grade non-Hodgkin's lymphoma. These cases may require doses up to 36 Gy, directed at a single site in a single phase, using 2D or 3D techniques with possible image guidance. MALT-omas of gastric or non-gastric origin, that are confined to the organs of involvement, may be treated with definitive radiation to doses of 36 Gy, using single site set-ups, with 2D or 3D techniques, single phase, with image guidance techniques. Extranodal NK/T-cell lymphoma, nasal lymphoma may require medically necessary radiation to a dose of 54 Gy – this may require IMRT techniques or 3D techniques, 30 fractions in two phases.

Radioimmunotherapy with either zevalin or bexxar is deemed medically necessary for patients with newly diagnosed or relapsed low grade B-cell lymphomas or transformed B-cell lymphomas that are CD20 positive. Radioimmunotherapy is medically necessary after at least a partial response to therapy, in patients with a baseline platelet count > 100K, and less than 25% marrow involvement. For patients with

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relapsed low grade B-cell lymphomas or transformed B-cell lymphomas that are CD20 positive, radioimmunotherapy is medically necessary after at least a partial response to therapy, in patients with a baseline platelet count > 100K, and less than 25% marrow involvement.
Adjuvant radiation after chemotherapy is medically necessary in many cases of patients with stage I-IIB disease, to areas of initial involvement, to doses of 36 Gy, up to 20 fractions with conventional schedule. 2D or 3D-conformal techniques, with image guidance, are considered medically necessary, directed at a single site in 1 phase. Adjuvant radiation after chemotherapy is medically necessary in some cases of patients with stage III-IV disease, to areas of less than a CR, to doses to 36 Gy, up to 20 fractions with conventional schedule. 2D or 3D-conformal techniques, with image guidance, are considered medically necessary, directed at up to 4 separate sites, in 1 phase apiece- IMRT is not considered medically neccessary. Sequential chemotherapy carries a high toxicity burden and requires substantial supportive care and the expertise of an experienced multidisciplinary team.

Radiation Therapy, palliative:

In patients with advanced or recurrent disease who are felt not to be curative, with symptomatic local disease, external beam radiation is indicated for symptom control. Up to 10 fractions are medically necessary, in one phase, using 2D or 3D techniques.

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Radiation Treatment of Lung Cancer

I. Non Small Cell Lung Cancer (NSCLC)

Work-up

A. CT of the chest including the upper abdomen (adrenal glands)
B. PET/CT for staging
C. MRI of the brain without and with contrast for Stage III NSCLC

POLICY

A. Definitive radiation therapy is medically necessary for patients with
   1. Stage III
   2. Stage I or Stage II [a or b]
      a. Surgery refused
      b. Medically inoperable
B. Pre-operative radiation therapy is medically necessary for patients with
   1. N2 disease clinically or by mediastinoscopy
   2. T3 or T4 primary lesion
C. Post-operative radiation therapy is medically necessary for patients with one or more
   1. N1 nodes positive
   2. Any mediastinal nodes positive for tumor
   3. No surgical sampling of mediastinal nodes
   4. Extra-capsular extension
   5. Margins of the resected specimen are positive or close
D. Palliative radiation therapy is medically necessary in patients with
   1. Stage IV disease and at least one of the following symptoms
      a. Airway obstruction
      b. Hemoptysis
      c. Pain
      d. Cough
      e. Endobronchial obstruction
      f. Superior vena cava obstruction or syndrome

Technique; 2D or 3D conformal techniques are considered medically necessary. IMRT is not considered medically necessary. Exceptions to the IMRT rule will be made on a case by case basis, especially in situations where there is disease in the bilateral mediastinum, in the para-spinal region, and for superior sulcus tumors. SBRT is considered medically necessary for patients with stage I or II tumors. Daily IGRT is not considered medically necessary for patients treated with 3D conformal technique.

II. Small Cell Lung Cancer (SCLC)

Work-up

A. CT of the chest including the upper abdomen (adrenal glands)

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B. MRI of the brain without and with contrast for limited stage

POLICY

Definitive radiation therapy is medically necessary for patients with
Limited stage- disease confined to one hemi-thorax –any T with NX, N0, N1 or N2 excludes N3
Technique - 2D or 3D conformal techniques are considered medically necessary. IMRT is not considered medically necessary. Exceptions to the IMRT rule will be made on a case by case basis, especially in situations where there is a need to treat the bilateral mediastinum, Daily IGRT is not considered medically necessary for patients being treated with 3D conformal technique.

A. Palliative radiation therapy is medically necessary for patients with
   1. Extensive stage SCLC- disease beyond one hemi-thorax including malignant pleural or pericardial effusion or hematogenous metastases, and one of the following symptoms
      a. Airway obstruction
      b. Hemoptysis
      c. Pain
      d. Cough
      e. Endobronchial obstruction
      f. Superior vena cava obstruction or syndrome
      g.

Technique – for palliative situations, up to 15 fractions in one phase will be considered medically necessary. IMRT is not medically necessary.

Prophylactic cranial irradiation is medically necessary in patients with good performance status.

Key Clinical Points:

Lung Carcinoma

Treatment of Stage III non-small cell lung carcinoma

Approximately one-third of patients with non-small cell lung carcinoma present with locally advanced disease that is considered unresectable, due to clinically apparent involvement of mediastinal lymph nodes or T4 disease. Until the mid-1990's, such patients were treated with radiation therapy alone. RTOG 73-01 was designed to assess optimal dose of radiotherapy for patients with locally advanced disease, including those with poor performance status and/or significant weight loss.[1] Local control and 2 year survival were better with 60Gy in 6 weeks compared with lower doses. The seminal study of Dillman, et al. from the CALGB was published in 1990 and was the first study to demonstrate a survival benefit with the use of induction chemotherapy followed by radiotherapy for patients with good performance status and weight loss of less than 5%.[2] Cisplatin-vinblastine for two cycles followed by thoracic radiotherapy to a dose of 60 Gy in 6 weeks was compared with the same radiotherapy alone in 155 randomized patients. Induction chemotherapy improved median survival, and 3 and 7 year overall survival. These results were confirmed in RTOG 88-08, a study of 452 patients with stage III NSCLC randomized to the positive arm of the CALGB trial (induction vinblastine-cisplatin followed by RT) versus hyper fractionated radiotherapy to 69.6Gy versus standard fractionation RT of 60Gy in six weeks.[3] These and other trials established the use of induction chemotherapy followed by standard fractionation radiation therapy as superior to radiation alone,

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and such therapy became the standard of care in the early 1990's for inoperable patients with stage III disease and good performance status. Use of concurrent chemo radiotherapy was also evaluated. RTOG 9410 is the largest trial assessing the value of concurrent versus sequential chemo radiotherapy.[4] In this trial, 610 patients with stage III disease were randomized to three arms: the positive arm of the CALBG trial reported by Dillman et al. (induction cisplatin-vinblastine for two cycles followed by RT to 63Gy) versus the same chemotherapy given concurrently versus a third arm of oral etoposide and weekly cisplatin given concurrently with 69.6Gy hyper fractionated RT (HART). Local control was better with concurrent HART, however the best survival was seen with concurrent cisplatin-vinblastine and standard fractionated RT. The use of concurrent radiotherapy was associated with a significantly increased acute esophagitis as compared to sequential therapy, and concurrent HART was associated with even more frequent severe esophagitis. Despite phase III data showing improved survival with the use of hyper fractionated radiotherapy compared with standard fractionation when radiation is used as the sole modality,[5] there has been difficulty transitioning this concept to the setting of concurrent chemotherapy, which is now the standard of care for patients with good performance status stage III disease.

The use of 3D-conformal techniques, which are now standard, has made possible a decrease in normal tissues receiving high doses. 3D conformal therapy techniques allow the development of complex multiple field radiotherapy plans that decrease the amount of normal tissue exposed to high doses. Better delineation of the target volume can be achieved with FDG-PET. If FDG-PET has not been done for prior staging purposes, use of FDG-PET for staging and radiation planning is appropriate. Incorporating the information from PET/CT can change the target volume in a significant proportion of patients as compared with CT alone. The radiotherapy target volume can decrease (due to the ability of PET to differentiate atelectatic lung from tumor) or increase (due to FDG uptake at mediastinal lymph nodes that were not positive by CT size criteria alone).[6, 7] In the increasingly common situation today when elective nodal irradiation is avoided, more accurate definition of involved sites of disease with PET decreases the likelihood that tumor bearing nodes will not be encompassed in the target volume.

The use of techniques that account for mobility of the tumor with respiration take on greater importance when 3D conformal treatment planning is utilized. By accounting for tumor motion on an individualized basis, smaller margins can be utilized thereby decreasing exposure to normal lung tissue. One approach to this problem is the use of respiratory gating or breath hold technique. Gating the treatment with the respiratory cycle or treating with breath hold can help to reduce the planning target volume or avoid marginal miss. Another method incorporates so-called 4D imaging. Use of rapid spiral CT scanning and acquisition of multiple images during breathing allows for better definition of the target volume, so that changes in the shape and location of the tumor during the breathing cycle can be taken into account in radiation delivery. With this technique temporal changes in tumor position and anatomy are incorporated into the treatment planning process. Radiotherapy delivery that adjusts in real-time to changes in tumor and normal anatomy, holds further promise to decrease the necessary tumor margin and exposure to uninvolved lung.

Use of Intensity Modulated Radiation Therapy (IMRT) is also being studied. With this technique, the intensity of the beam is spatially varied in real time and delivery is accomplished using multiple fields at different angles or with rotational arc therapy. The primary disadvantage is that a greater volume of normal tissue gets low doses. Since the normal lung has low tolerance to even small doses, this technique is not appropriate in the majority of cases of locally advanced non-small cell carcinoma. In rare cases, IMRT may

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offer advantages in the treatment of patients with bilateral mediastinal nodal involvement or in patients treated with definitive radiotherapy (without surgery) for superior sulcus tumors, although this has not been systematically studied.

Pre-operative and post-operative therapy

Patients with stage IIIA disease on the basis of ipsilateral mediastinal nodal involvement have traditionally been considered unresectable, as outcome with surgery has generally been poor for patients with clinically apparent mediastinal involvement, particularly when multiple station N2 disease is present. However, with improvements in modern staging and more generalized use of multimodality therapy, there may be subsets of patients with clinical N2 disease who might benefit from surgery. Attempts have been made to "downstage" patients with pre-operative chemo radiotherapy. The dose of radiation in the pre-operative setting is generally 45Gy in 25 fractions. 3D-CRT techniques may be helpful, even at these lower doses, to reduce the dose to normal lung. Similarly, respiratory gating techniques may also be helpful, particularly for lower lobe primary tumors.

Post-operative radiotherapy improves loco regional control as demonstrated by an early trial conducted by the Lung Cancer Study Group; however this did not translate into an overall survival benefit.[8] Enthusiasm for post-operative radiotherapy diminished after the publication of the PORT meta-analysis, which included 2,128 patients with stage I to III non-small cell lung carcinoma enrolled on 9 randomized trials from 1966-1994.[9] In the entire group of patients, there was a 7% absolute reduction in survival for patients who received radiotherapy. The trials included in the meta-analysis have a variety of serious pitfalls, including the inclusion of ineligible patients, inadequate staging work-up, inclusion of node negative patients, and RT techniques that today would be expected to produce deleterious outcomes. Most of the trials used excessive total dose (>50 Gy) or high dose per fraction (e.g. 2.5 Gy per fraction). In many of the trials, lateral fields were used, which exposes a significant volume of normal lung to intolerable radiation doses. Additionally, systemic therapy was not used, and improved local control is more likely to translate into a survival benefit if effective systemic therapy is available. Patients with N2 disease are likely to achieve a significant local control benefit from post-operative radiation, and with modern techniques these patients may accrue a survival benefit. An American Intergroup trial and an EORTC trial are presently underway to re-evaluate the role of radiotherapy for patients with N2 disease.

Prophylactic Cranial Irradiation (PCI) for NSCLC

Twenty to 50% of patients with clinical stage III non-small cell lung carcinoma will develop brain metastases during the course of the disease and in patients who have responded to prior multimodality therapy, a significant proportion experience relapse in the brain as the first or isolated site of failure.[10] Early trials of PCI showed greater than 50% relative risk reduction in the incidence of brain metastases with PCI, however this did not translate into a survival benefit in any of the trials.[11] Concerns of neurocognitive morbidity from PCI are largely related to the early experience with the use of PCI for small cell carcinoma, which is associated with a significant proportion of patients having neurocognitive dysfunction prior to radiation. More modern trials that employ lower dose per fraction and avoid concurrent chemotherapy have not found any impact of PCI on neurocognitive function.[12] The RTOG is presently conducting a study of patients with stage III non-small cell carcinoma who do not have progressive disease to evaluate the potential benefit of PCI. Patients will be randomized to 30Gy in 15 fractions versus observation after definitive local therapy. The primary endpoint is survival, and secondary endpoints are the rate of CNS

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metastasis, quality of life, and neurocognitive effects. Outside of a clinical trial, prophylactic cranial irradiation is not appropriate.

Early Stage NSCLC

Radiation therapy is appropriate for curative intent treatment of patients with stage I and II NSCLC who are medically inoperable. Patients with hilar nodal involvement should be treated with standard fractionation (e.g. 60Gy in six weeks) and 3D-CRT techniques are preferred if available. For node negative stage IA and IB non-small cell lung cancer in patients who are medically inoperable or who refuse surgery, Stereotactic Body Radiotherapy (SBRT) is an appropriate option. Stereotactic Body Radiotherapy (SBRT) is a technique that uses multiple intersecting beams of radiation to deliver a very high radiation dose to a precisely defined area, while minimizing radiation to surrounding areas. Precise immobilization techniques are required to deliver SBRT. Treatment is generally delivered in 3-5 fractions. A linear accelerator can be used to deliver stereotactic radiotherapy. The CyberKnife™ is a robotic version that can be used to treat any part of the body. Stereotactic Body Radiotherapy (SBRT) is an appropriate technique for patients with node negative peripheral lung cancers less than 5cm in maximum dimension.[13] Patients with central tumors can experience excessive toxicity when higher fraction sizes and fewer fractions (e.g. 3) are utilized.[14] Use of Mediastinoscopy is appropriate for staging of clinical stage T2N0 patients prior to definitive SBRT. Image Guidance Radiation Therapy (IGRT) may also improve the therapeutic ratio. Accurate patient set-up with the use of radiopaque markers placed in the tumor or use of daily CT scan imaging can essentially eliminate any additional margin that might otherwise be needed for daily patient set-up variability.

Palliative treatment (reference 25)

Some patients with localized disease but with significant co-morbidities, poor performance status, or significant weight loss may be appropriate for radiation as definitive treatment with a hypo fractionated schedule, use of split-course treatment, or use of more conventional fractionation RT alone (e.g. 60Gy in 6 weeks). In addition, RT is effective in the palliation of symptoms due to local tumor, such as hemoptysis, cough, or imminent endobronchial obstruction. Approximately 40% of patients with NSCLC present with stage IV disease. One multi-institutional phase III randomized study examined a variety of fractionation schemes including 40Gy split course, 30Gy in 10 fractions, and 40Gy in 20 fractions.[15] There was no difference between arms and 60% of patients achieved symptom relief. Bezjak et al. reported a randomized phase III trial of 231 patients to 20Gy in 5 fractions versus 10Gy in one fraction. Similar palliation was seen in both arms, although patients in the 20Gy arm have longer median survival.[16] The Medical Research Council compared 17Gy in 2 fractions (one per week) with 30Gy in 10 fractions over 2 weeks.[17] There was no difference in survival or palliation of symptoms. Hemoptysis was relieved in 86% of patients, cough in approximately 60% of patients, and pain in approximately 50% of patients. Therefore, data supports the use of short hypo fractionated regimens, and there is generally no general role for more protracted schemes beyond 30Gy in 10 fractions. Endobronchial (EBB) radiation has also been found in retrospective studies to be effective in the palliation of symptoms due to intraluminal tumor, including obstruction, dyspnea, and cough. The procedure requires bronchoscopic guidance of the brachytherapy catheter. There is no proven role for more than 3 applications. EBB will be considered medically necessary after a failed course of external bean radiation therapy.

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Small Cell Carcinoma

There is little role for surgery in the management of patients with SCLC. In rare cases of clinical stage T1-T2N0 disease, surgery establishes the diagnosis and effectively removes the primary tumor. Such patients should also be staged with mediastinoscopy, and if mediastinal lymph nodes are negative, chemotherapy alone can be entertained. Radiotherapy improves survival of patients with limited stage SCLC.[18] Early concurrent chemo radiotherapy leads to improved survival as compared with sequential therapy.[19] Standard radiation fractionation consists of either 45Gy given at 1.5Gy bid (hyper fractionation)[20,21] or at 1.8 to 2.0Gy per day to 54-70Gy. Local thoracic radiotherapy for patients with extensive stage disease is not an established approach, however, in selected patients it may be considered, such as those with clinically apparent disease only at the primary site and complete response elsewhere.

More than 50% of patients with SCLC will experience brain metastases during the course of disease. Prophylactic cranial radiotherapy reduces this risk by approximately 50% in relative terms, and improved overall survival in patients with chemo-responsive limited stage SCLC.[22] and extensive stage SCLC.[23] Concerns regarding neurocognitive defects are obviated by avoiding high dose per fraction treatment and concurrent chemotherapy. PCI is not appropriate for patients with severe co-morbidities, those who are bedridden most of the time, or those with severely impaired cognitive functioning. The standard dose/fractionation for PCI is 25Gy in 10 fractions.[24]

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Radiation Treatment of Pancreas Adenocarcinoma

Radiation technique typically involves the use of 4-6 fields to encompass the regional nodes and primary tumor site. Customized blocking is utilized. 3-D conformal therapy is appropriate, which utilizes CT-based simulation and a 3-D workstation to design the radiation fields. IMRT may be considered, particularly in the post-operative setting, if necessary, to respect the tolerance of the surrounding normal structures, notably small bowel which could have been affected by surgery. IMRT may not be necessary in the neoadjuvant setting for doses in the region of 50.4 Gy where dose restraints should be met using 3D conformal techniques. IMRT may be considered medically necessary in the definitive treatment of pancreatic cancer (no surgery). Although dose response has not been proved, IMRT may be necessary when higher doses are delivered. For palliation, IMRT is not considered medically necessary.

POLICY

The use of external beam radiotherapy is considered medically necessary in the following clinical situations

A. Unresectable disease
    1. Curative treatment in conjuction with chemotherapy
B. Borderline resectable disease
    1. Neoadjuvant treatment in conjuction with chemotherapy
C. Resected disease
    1. Must be post surgical
    2. Chemoradiation planned
D. Palliative
    1. Curative treatment will not be planned
    2. Metastatic disease is documented

Technique – 3D conformal technique is considered medically necessary for A-D. IMRT is considered medically necessary for A-C when 3D conformal techniques are unable to produce dosimetry that is considered relatively safe with respect to critical organs. For palliative situations, up to 15 fractions in one phase is considered medically necessary. IMRT is not considered medically necessary.

Key Clinical Points:

Pancreatic cancer is the fourth leading cause of cancer mortality in the United States. Surgical resection is integral to the curative management of pancreatic cancer. Unfortunately only twenty percent of patients present with resectable disease. Resectability is typically defined by a lack of encasement of the superior mesenteric vein and portal veins and clear fat planes around the celiac artery, superior mesenteric artery and hepatic artery. Borderline resectability generally includes involvement of superior mesenteric vein or portal vein, but lack of encasement of the adjacent arteries. Patel et al[18] have reported on the use of neoadjuvant chemotherapy and IMRT to improve the likelihood of successful complete resection. In their study, 8 of 17 borderline resectable patients achieved negative margin resection after neoadjuvant therapy.

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The underpowered but landmark Gastrointestinal Tumor Study Group (GITSG) study established the role of postoperative chemoradiation by demonstrating a survival benefit with this treatment strategy.[1] The GITSG study included 43 patients, randomized to surgery alone or surgery followed by chemoradiation. This trial used a 40 Gy split course regimen that is rarely used today. Though underpowered, there was a 5-year improvement in overall survival. Studies from the Mayo Clinic and Johns Hopkins have supported the use of chemoradiation following resection. The Mayo Clinic study retrospectively reviewed 472 patients.[2] The Johns Hopkins study included 616 patients.[3] Both studies demonstrated improved 5-year overall survivals in the cohorts receiving chemoradiation. A Johns Hopkins- Mayo Clinic Collaborative Study analyzed patients receiving adjuvant chemoradiation compared with surgery alone.[4] In a retrospective review of 1,045 patients with resected pancreatic cancer, 530 patients received chemoradiation. Median and overall survivals were significantly improved in the chemoradiation group. In contrast the heavily criticized European Organization for Research and Treatment of Cancer (EORTC) and European Study Group for Pancreatic Cancer (ESPAC) studies have not supported the use of adjuvant chemoradiation.[5,6] These studies were heavily criticized for trial design, inclusion of more favorable histologies, lack of quality assurance, and use of split course radiation.

Following surgical resection, chemotherapy alone or chemoradiation may be the appropriate course of action.[7] In borderline resectable patients, radiation is often utilized in the neoadjuvant setting in conjunction with chemotherapy.[7] In unresectable patients, radiation is generally used as definitive treatment usually in conjunction with chemotherapy.[7] A GITSG study of 194 patients with unresectable pancreatic cancer, randomized patients to 60 Gy of radiation alone, split course 40 Gy with concurrent 5-FU, and split course 60 Gy with concurrent 5-FU.[8] Survival was improved in the chemoradiation arms with one-year survival rates of 38% and 36%.

Three-dimensional techniques are critical to respect the radiation tolerance of the surrounding critical structures, notably the kidneys, liver, small bowel and spinal cord. Dose prescription is typically 50.4-60 Gy, and generally involves a conedown following 45 Gy. Dose escalation studies are under investigation. IMRT has increasingly been employed to decrease radiation dose to surrounding critical structures, in particular the kidneys, liver, small bowel and spinal cord, and dosimetric studies have confirmed significantly lower doses to these structures with IMRT compared to 3D techniques.[19] IMRT is associated with a statistically significant decrease in acute upper and lower GI toxicity among patients treated with chemoradiotherapy for pancreatic/ampullary cancers.[20] Based on these studies, IMRT is considered medically necessary in the treatment of pancreatic cancer in the definitive and adjuvant settings, when dose constraints to organs at risk cannot be met with 3D conformal techniques. When using IMRT in the upper abdominal region, the uncertainty inherent due to organ motion underscores the utility of image guidance. Respiratory gating techniques are often used with both 3D-CRT and IMRT.

The benefits of dose escalation with both 3D-CRT and IMRT techniques are under investigation and thus far inconclusive. The aforementioned landmark GITSG study did not demonstrate a meaningful improvement in survival for the cohort receiving 60 Gy split-course with concurrent 5-FU compared with 40

Gy split-course with concurrent 5-FU. [4,8] A phase III trial of locally advanced unresectable pancreatic cancer, compared intensive induction chemoradiotherapy consisting of 60 Gy, 5-FU and CDDP followed by maintenance gemcitabine, to gemcitabine alone.[9]

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Survival was improved in the gemcitabine alone arm. One year OS was 32% in the chemoradiotherapy cohort vs. 53% in the gemcitabine alone arm. There was greater grade 3 and 4 toxicity in the chemoradiotherapy arm. A phase II study from the Netherlands analyzed the feasibility of dose escalation in locally advanced unresectable pancreatic cancer, treated with radiation alone.[10] Forty-one patients were treated with 3D-CRT in doses of 70-72Gy. The median survival was 11 months with acceptable toxicity. RTOG 8801 was a phase I/II trial of localized unresectable pancreatic cancer.[11] Treatment consisted of 61.2 Gy with CI 5-FU, prophylactic hepatic irradiation, followed by 6 months of 5 FU. Seventy-nine patients were evaluable with a minimum follow up of 8.2 months. Thirty-one patients had severe grade 3 toxicity. Persistent or progressive pancreatic cancer was noted in 73%. Median survival was 8.4 months.

There is no clear consensus regarding the appropriate maximum dose when utilizing IMRT. Fuss et al retrospectively reviewed 41 patients undergoing ultrasound based image guided IMRT for pancreatic cancer.[12] The mean total dose was 55 Gy (range 45-64Gy). Grade 3 toxicity was 7.3%. Actuarial one- and two-year survival were 38% and 25%, respectively, comparable to published survival data. Brown et al reviewed dose escalation in unresectable pancreatic cancer comparing 3D-CRT, sequential IMRT boost and integrated IMRT boosts techniques.[13] In 15 patients, treatment plans were generated and dosimetric analysis performed at doses of 54 Gy, 59.4 Gy and 64.8 Gy. Doses to the kidney, small bowel, liver and spinal cord were analyzed as well as target coverage. The authors concluded that the integrated boost IMRT technique allowed dose escalation to 64.8Gy with acceptable normal tissue doses. Cost, as well as increased effectiveness of IMRT has been questioned.[17] Continued investigation of radiation dose escalation in the setting of clinical trials is warranted. Dose escalation studies investigating IORT, radiosurgery, and brachytherapy are ongoing.

Cyberknife (Accuray Inc, Sunnyvale, California) is under active investigation, revealing promising local control results. Koong et al[14] in a phase I trial, treated locally advanced tumors with a single fraction of Cyberknife. Tumors measured less than 7.5 cm. Elective lymph nodes and regions were not treated. Dose was escalated starting at 15 Gy and then 20 Gy. The trial was terminated at 25 Gy achieving 100% local control. Median overall survival was 11 months with a high rate of distant metastasis. In a subsequent Phase II trial, Koong et al[15] studied Cyberknife as a 25 Gy boost, one month following a course of conventional IMRT to 45 Gy with concurrent 5FU, delivered to the tumor and regional lymph nodes. Local control was 94%. Median overall survival was 33 weeks. Toxicity included a significant amount of duodenal ulcers 4-6 months following treatment. Koong et al continued investigation of Cyberknife in a prospective study evaluating a 25 Gy single fraction of Cyberknife delivered between 2 cycles of Gemcitabine.[16] Sixteen patients with locally advanced pancreatic cancer were treated to the gross tumor volume with a 2-3 mm margin. Gemcitabine was continued until progression or dose limiting toxicity. Nineteen % developed local disease progression. Median survival was 11.4 months. Late gastrointestinal toxicity was common with a high rate of duodenal ulcers.
At this time, in view of the relatively high complication rates with hypofraction, cyberknife treatment for pancreatic cancer is considered investigational.

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Radiation Treatment of Prostate Cancer

POLICY

Radiation therapy is considered medically necessary in the following situations

A. External Beam Radiation Therapy (EBRT) as monotherapy (3D conformal, Intensity Modulated Radiation Therapy (IMRT), Image Guided Radiation Therapy (IGRT), or Stereotactic Body Radiosurgery (SBRT))
   1. Clinically localized disease
      a. Stage less than T3a
      b. Gleason score <8
      c. PSA <20
   2. Life expectancy >5 years
   3. Negative bone scan within the last 6 months (Bone scans not recommended for patients with low risk prostate cancer – PSA<10 + GS <7 and stage 1c/2a)

B. External Beam Radiation Therapy (EBRT) in postoperative setting (3D conformal or Intensity Modulated Radiation Therapy (IMRT) or Image Guided Radiation Therapy (IGRT)
   1. Negative bone scan within the past 6 Months
   2. Positive surgical margins
   3. Extracapsular extension
   4. Seminal vesicle involvement
   5. Positive lymph nodes
   6. Gleason score 9 or 10
   7. Detectable or rising postoperative PSA level
   8. Prostate cut-through

C. Brachytherapy- monotherapy or combined with External Beam Radiation Therapy (EBRT) (3D conformal or Intensity Modulated Radiation Therapy (IMRT) or Image Guided Radiation Therapy (IGRT)
   1. Clinically localized disease
      a. Stage <T3a
      b. Gleason score <8
      c. PSA <20
   2. Life expectancy >5 years
   3. Negative bone scan within the last 6 months

D. Brachytherapy as combination therapy
   1. Intermediate to high risk prostate cancer

NOTE – EBRT plus implant is not considered medically necessary in patients with low risk disease

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Key Clinical Points:

Brachytherapy

Brachytherapy is one type of radiation therapy used to treat prostate cancer. Unlike External Beam Radiation Therapy (EBRT), in which high-energy x-ray beams generated by a machine are directed at the tumor from outside the body, brachytherapy involves placing radioactive material directly inside the prostate. This can be accomplished by performing a permanent seed implant by injecting radioactive seeds directly into the prostate gland, and typically using either Iodine or Palladium seeds. As part of the post-implant evaluation of the adequacy for the implant, a single CT scan of the prostate is performed approximately one month after the implant to determine the dosimetric quality of the implant, so that decisions about the potential need for additional therapy can be made. High-dose-rate brachytherapy, as opposed to permanent low dose seed implants, uses temporary radioactive sources. Needles are placed into the prostate gland. A high activity radioactive seed (Iridium-192) is directed to predetermined positions in these needles for precalculated dwell times via a remote after loading system, and after the appropriate dose is delivered the needles are removed, usually within 24 hours.

Brachytherapy, either as monotherapy or combined with external beam radiotherapy, may be appropriate depending on the clinical situation. The resurgence of interest in prostate brachytherapy is principally due to the evolution of transrectal ultrasonography, the development of a closed transperineal approach, and sophisticated treatment planning software. These imaging and planning advances dramatically improved the accuracy of seed placement. In addition, CT based postoperative dosimetry provided the ability to evaluate implant quality and proactively influence outcome. Brachytherapy as monotherapy is well established for low risk prostate cancer. Permanent prostate brachytherapy is a highly efficacious treatment for clinically localized prostate cancer with biochemical outcomes and morbidity profiles that compare favorably with those of competing local modalities8,9. HDR monotherapy may also be appropriate in selected cases.

A modest amount of data has been published from single institutions and in small prospective studies on the strategy of combining EBRT with either a low- or High-Dose-Rate (HDR) brachytherapy boost for patients with intermediate to high-risk prostate cancer [10-17,] and is considered appropriate. However, such combination therapy is generally inappropriate for low risk patients.

Conventional External Beam Radiation Therapy

Conventional External Beam Radiation Therapy (CRT) is a method for delivering a beam of high-energy x-rays to the location of the patient's tumor. The beam is generated outside the patient, usually by a linear accelerator and is targeted at the tumor site. With careful planning the tumor cells are destroyed and the surrounding tissue is spared from the harmful effects of the radiation. No sources are placed inside the patient's body. CRT refers to a treatment planning method wherein the prostate and other target tissues are identified by surrounding anatomy such as bony landmarks and contrast enhanced viscera. This is considered “2D” planning (plain films are used) and is generally not considered appropriate for the definitive treatment of prostate cancer especially in cases of locally advanced or higher risk prostate cancer where higher doses of radiation are usually delivered (ACR appropriateness Criteria).[1]

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Three-Dimensional Conformal Radiation Therapy

Three-Dimensional Conformal Radiation Therapy (3D CRT) is an advanced form of external beam radiation that uses CT and computers to create a 3D picture of the tumor so that multiple radiation beams can be shaped exactly to the contour of the treatment area.[2]

Intensity Modulated Radiation Therapy

Intensity Modulated Radiation Therapy (IMRT) employs a very sophisticated computerized 3D treatment-planning system that accurately delivers a high dose of radiation to tumors of varying shapes with even more accurate sparing of surrounding tissue than can be accomplished with 3D CRT. IMRT evolved out of the inability of 3D CRT to irradiate tumors that are concave, surrounded by normal tissue, or in very close proximity to sensitive normal tissue, without causing excessive radiation exposure of adjacent normal tissue. IMRT incorporates two distinct features over 3D CRT; inverse treatment planning and computer-controlled intensity modulation of the photon radiation beam. IMRT is high precision treatment that utilizes computer controlled linear accelerators to deliver precise radiation doses to the 3D shape of the tumor. This results in sparing surrounding normal tissue and ultimately limiting side effects.

Radiation therapy directed to the prostate is generally not appropriate in men with distant metastatic (stage M1) disease. IMRT is covered as medically necessary for patients with non-metastatic prostate cancer when there is a reasonable concern about damage to the surrounding normal tissue with the use of conventional external beam radiation therapy or 3D conformal radiation therapy. Guidelines on prostate cancer from the National Comprehensive Cancer Network (NCCN) in 2010 state that 3D and IMRT techniques should be employed in preference to conventional techniques in the treatment of prostate cancer. Doses of 75.6-79 Gy in conventional 36-41 fractions to the prostate (+/- seminal vesicles for part of the therapy) are appropriate for patients with low-risk cancers. For patients with intermediate or high risk disease, doses between 78-80+ Gy improved PSA-assessed disease control. Image guided radiation therapy (IGRT) techniques employing ultrasound, implanted fiducials and KV imaging, or cone beam CT is required if dose is >78 Gy and is strongly encouraged if doses >75 Gy are used.

In order to ensure that disease is localized prior to delivering high dose radiotherapy, a bone scan must be obtained within the 6 months leading up to radiotherapy in patients with “advanced disease”. This includes all patients with stage ‘T3a’, ‘T3b’, or ‘T4’, Gleason score 8 through 10, or PSA >20 ng/ml. All patients being considered for postoperative radiotherapy must also have a bone scan.

Standard external beam radiation courses span up to 9.5 weeks (maximum 48 fractions). There may be radiobiologic benefits to using larger doses per fraction and hypofractionated courses.
A phase is defined as a distinct change in the target volume, and phases are delivered sequentially. Low risk patients, defined as stage ‘T1a’ , ‘T1b’, ‘T1c’, or ‘T2a’, Gleason score of 6 or less, PSA level 10 ng/ml or less, and fewer than 50% of biopsy cores involved (modified from D’Amico 2002) 4 are treated with one or two phases (one directed to the prostate and seminal vesicles, and another to the prostate alone). In selected intermediate or high risk cases, another phase encompassing the pelvic lymph nodes may be appropriate. When IMRT or 3D CRT is delivered using multiple gantry angles, use of more than nine gantry angles per treatment phase/target volume is unlikely to provide clinically meaningful improvements in dose distribution and can create greater inhomogeneity within the target. There is also concern over the longer treatment time.. When indicated, Image Guided Radiation Therapy (IGRT) with cone beam CT, KV imaging or ultrasound may be appropriate to ensure accurate daily setup. In prostate cancer, KV imaging for IGRT is only considered appropriate when fiducial markers implanted into the prostate gland are used.

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Stereotactic Body Radiosurgery (SBRT)

The ASTRO Consensus panel statement from April 2010[18] on the use of stereotactic body radiotherapy approaches (5 fractions or less) states"results, primarily available only in abstract form and consisting of reports of clinical experiences from single institutions, show that SBRT for the prostate is technically feasible, with little reported acute morbidity. Very early results, of limited statistical power, suggest that treatment will induce an initial PSA response of a magnitude equivalent to that seen with conventionally fractionated radiotherapy. Since the publication of the ASTRO consensus panel, there have been many more publications on the outcome and toxicity of SBRT for prostate cancer (references 19-38). " The data confirms that PSA relapse-free survival and acute and chronic toxicity are equivalent with those of conventional external beam radiation therapy or permanent brachytherapy, in publications now with medium follow-up beyond 5 years. Although late outcome and toxicity data beyond 10 years are not yet available, SBRT for low and intermediate risk prostate cancer, in selected and well-informed patients, will be considered an acceptable first line of treatment.

Post-operative Radiation Therapy

In the setting of postoperative prostate cancer,[5, 6, 7] radiation therapy may be beneficial in the setting of positive margins, extracapsular extension, seminal vesicle involvement, lymph node involvement, or prostate cut-through. In addition, a patient with a detectable or rising postoperative PSA level, or a Gleason score 9 or 10 tumor, may benefit from postoperative radiotherapy. In the postoperative setting, the treatment course generally does not exceed 8 weeks (maximum of 42 fractions).

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Radiation Treatment of Rectal Cancer

Colorectal cancer is the third most commonly diagnosed cancer in the United States. Surgical resection plays a key role in treatment. The surgical approach depends on the extent and stage of disease. Transanal excisions are used for early stage lesions. Other transabdominal approaches include low anterior resections, total mesorectal excisions, and abdominal perineal resections. The Swedish Rectal Cancer Trial demonstrated an overall survival advantage to preoperative radiation. The German Rectal Cancer Study Group investigated preoperative chemoradiation compared with postoperative therapy. Preoperative chemoradiation showed decreased local recurrence rates and improved sphincter function. Radiation is utilized in the neoadjuvant, adjuvant, palliative and medically inoperable settings.

Radiation technique typically involves the use of 4 fields to encompass the regional lymph nodes and primary tumor site. Customized blocking is utilized. 3-D conformal therapy is appropriate, which utilizes CT-based simulation and a 3-D workstation to design the radiation fields. A dose of 45-54 Gy in 25-30 fractions over 5-6 weeks is commonly used.

POLICY

Radiation therapy is considered medically necessary in the following clinical situations

A. Surgical candidate
   1. Preoperative
   2. Postoperative
B. Inoperable

   Treatment technique – 3D conformal techniques are considered medically necessary. IMRT in the pre- and post-operative settings should only be used in the setting of an IRB approved clinical trial. Consideration may be given to the use of IMRT in select cases of locally and regionally advanced cancer when higher doses of radiation may be necessary.

C. Palliative
   Treatment technique – up to 20 fractions in one phase using 2D or 3D technique is medically necessary. IMRT is not medically necessary.

Key Clinical Points:

Based upon established criteria, assessment of peer-reviewed literature, and consensus present in established guidelines (ACR/ASTRO, NCCN), radiation therapy is considered an integral component in the multidisciplinary management of rectal cancer. The rectum extends from the transitional zone of the dentate line to the sigmoid colon. Tumors extending below the peritoneal reflection are considered rectal, while more proximal tumors are considered colonic.

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Workup:
Work-up of patients with rectal carcinoma includes digital rectal exam and rigid proctoscopy. Laboratory studies including CBC, comprehensive metabolic panel, and CEA are performed. Patients with a significant family history should be considered for genetic counseling. Biopsy is performed to establish the diagnosis and histology. Complete colonoscopy is indicated to assess for additional bowel cancers. In order to rule out metastatic disease, contrast enhanced CT of the chest, abdomen, and pelvis is indicated. Endorectal ultrasound and/or MRI of the pelvis are appropriate to assess the extent of pelvic disease and nodal metastases. Establishing the stage of disease, its potential for resection, and the patient's anticipated ability to withstand radiation therapy and chemotherapy are all part of the initial evaluation.

Treatment:
Treatment of rectal cancer requires interdisciplinary interaction between the radiologist, gastroenterologist, colorectal surgeon, radiation oncologist, and medical oncologist. Surgical treatment can range from polypectomy for selected T1 tumors, Transanal local excision for selected patients with low risk T1/T2 tumors in the absence of positive margins, lymphovascular invasion (LVI), or high grade. For patients who have T2 primary and negative margins, postoperative chemoradiation is appropriate after transanal execision. For patients with T3 primary or positive nodes total mesorectal excision (TME) either by low anterior resection (LAR) or abdominoperineal resection (APR), depending on the proximity of the tumor to the anal verge.

Based on earlier randomized trial data, the NIH Consensus Conference of 1990 recommended post-operative chemoradiotherapy for patients with T3 and/or node positive disease (1). More recent trials of preoperative chemoradiation have established that as the preferred approach. Preoperative therapy affords the opportunity for downstaging of the tumor, improved resectability, greater likelihood of sphincter preservation, and improved local control (2). Patients who present with synchronous limited metastatic disease amenable to R0 resection may also be candidates for definitive post-operative chemoradiation. Patients with isolated pelvic or anastomotic recurrence who have not received prior radiation may be appropriately treated with pre-operative or post-operative chemoradiation with or without intraoperative radiation or with primary chemoradiation if deemed unresectable.

Radiation Treatment Techniques and Schedules
Various treatment techniques may be used to decrease complications, such as prone positioning, customized immobilization (e.g. belly boards), and the use of multiple fields and incorporation of three-dimensional treatment planning. Intensity modulated radiotherapy and image guidance are not medically necessary except in rare extenuating circumstances where higher doses are required (e.g. unresectable cases or those with positive margins) and normal tissues such as small bowel cannot be adequately spared. For unresectable cancers or patients who are medically inoperable, doses higher than 54 Gy may be appropriate. In the preoperative setting a dose of 50.4 Gy in 28 fractions is appropriate. In the postoperative setting with negative margins, 54 Gy in 30 fractions may be appropriate. Patients with positive margins may require doses higher than 54Gy.

Radiation Therapy, palliative:
In previously un-irradiated patients with unresectable metastatic disease and symptomatic local disease or near obstructing primaries, and who have reasonable life expectancy, external beam radiation may be appropriate. Up to 20 fractions are medically necessary, in one phase.

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Radio-Immunotherapy

See Non-Hodgkin's Lymphoma policy.

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CCN Hyperthermia Policy

CCN Policy

I. Indications for the use of hyperthermia and concurrent radiation therapy treatment
   A. Superficially recurrent melanoma
   B. Chest wall recurrence of breast cancer
   C. Recurrent cervical lymph nodes from head and neck cancer
   D. No evidence of metastatic disease for which systemic chemotherapy or hormonal therapy is being given concurrently or planned.
   E. No evidence of depth of tumor recurrence greater than 4 cm.
   F. No more than 10 hyperthermia treatments delivered two times per week at 72- hour intervals

II. The use of intraluminal, endocavitary ,interstitial, regional deep tissue hyperthermia exceeding 4 cm. in depth and whole body hyperthermia are considered investigational

Background

After initial enthusiasm for the use of hyperthermia in the late 1970's, interest waned with the publication of studies showing little or no benefit in the mid- 1980's. Later review of the negative findings, disclosed that the critical temperature necessary for hyperthermic cell death, 42 to 43 degrees centigrade, was either poorly measured or poorly maintained in these studies. Indeed, point measurements rather than volume mapping of thermal gradients were relied upon in planning these hyperthermia studies.

Renewed interest in the use of hyperthermia began to emerge both in Europe and the U.S. in the 1990's. Research from Duke, Northwestern University, University of Southern California, Stanford University, Washington University, as well as centers in Holland, Germany, Norway, Austria, Italy and Switzerland have contributed substantially in the emergence of hyperthermia as a useful treatment modality when combined with radiation therapy.

Currently, in the U.S., the FDA has approved hyperthermia for use in the treatment of cancer when combined with radiation therapy for the " palliative management of certain solid surface and subservice malignant tumors (i.e. melanoma, squamous or basal cell tumors, adenocarcinoma, or sarcoma) that are progressive or recurrent despite conventional therapy. " The National Cancer Center Network recommends "that the use of hyperthermia be limited to treatment centers with appropriate training, expertise and equipment. " The NCCN Panel on Breast Cancer concluded that it was a controversial Category 3 recommendation in the treatment of local or regional recurrent breast cancer.

Following FDA approval, Medicare approved coverage for local hyperthermia when used together with radiation therapy. The use of hyperthermia alone or in conjunction with chemotherapy has not yet been approved. Coding for this treatment is recognized and published in the current 2010 ACR/ASTRO guide. Private insurers including AETNA, national BCBS centers and others have followed suit in their recognition and payment for this modality.

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Although research into hyperthermic treatments at depths greater than 4cm. is ongoing in the U.S., it is currently recognized only as investigational as are intraluminal, endocavitary, and interstitial applications. In May 2009, the FDA granted HUD (Humanitarian Use Device) status to the BSD 2000 for the treatment of cervical cancer patients ineligible for chemotherapy (treatment population less than 4,000). This is the only approval for deep heating and only actual costs incurred in the research may be billed. Other applications for deep heating are pending for both BSD and Medifocus devices.
In the U.S. , only the BSD-500 has FDA commercial clearance for superficial heating (less than a 4 cm. depth). This is currently the only device approved for reimbursement. It operates at the microwave range of 915 MHz with different applicators and power setting ranging from 20 to 250 Watts. The standard recommended treatment regimen for use with radiation therapy is a " total of 10 hyperthermia treatments delivered two times per week at 72-hour intervals, with each heat treatment preceded or followed by a standard prescribed dose of ionizing radiation within 30 minutes of the heat treatment. " A sustained intratumoral temperature of 42.5 degrees Centigrade for 60 minutes is recommended.

Key clinical data

There are 3 clinical sites in which randomized studies have documented the benefit of hyperthermia given in conjunction with radiotherapy.

1. Melanoma – 134 metastatic or recurrent lesions of malignant melanomain 70 patients were randomly assigned to receive radiotherapy (three fractions of 8 or 9 Gy over 8 days) alone or followed by hyperthermia (43 degrees C for 60 min.). [1] Beneficial local effect was 28% for radiation alone, and 46% for combined treatment. Toxicity was not higher with hyperthermia.
2. Breast – 5 randomized trials were combined to report the benefit of combined treatment for superficial localized breast cancer. Control rate for RT alone was 41%, while that for combined treatment was 59%.[2] The greatest effect was observed in patients with recurrent lesions in previously irradiated lesions where further irradiation was limited to low doses.
3. Head and neck metastatic lymph nodes – a randomized study of 44 nodes in 41 patients confirmed the improved 5 year actuarial nodal control of the combined treatment arm. In addition, the study reports a statistically significant in survival at 5 years, and no increased toxicity from combined modality therapy. [3]

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CCN Policy on the use of Neutron Radiotherapy in Cancer Treatment

Introduction:

Neutron beam treatment differs from other forms of radiation particle treatment such as protons or electrons as they have no electrical charge. The treatment effects are the results of the neutron mass producing dense radiation energy distributions. This effect is high energy linear transfer (LET) and may offset the negative effects of low oxygen tension in tumors leading to increased rate of control in hypoxic tumors. Currently, the number and location of neutron facilities in the U.S. is quite small. This has limited research and has resulted in a lack of substantial information on its clinical effectiveness, although it has been tried in soft tissue sarcoma, prostate cancer, pancreas, colon and lung cancers amongst others. The lack of data and comparative trials limits its designation to investigational and experimental with the exception of salivary gland cancers.

Indications:

Neutron beam treatment is considered medically necessary for salivary gland cancers that are inoperable, recurrent, or are resected with gross residual disease or positive margins.

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Proton Beam Therapy

Proton beam therapy is a form of external beam radiation therapy also known as charged particle therapy. Proton beam therapy (PBT) provides the opportunity of achieving dose escalation and decreasing toxicity by delivering physical dose to a narrowly defined region, while avoiding normal tissue. The potential benefit is to improve local control, improve survival, and decrease toxicity.

While PBT has been used in patients in the United States since the mid 1950's, and although it has been shown to be effective in many malignancies, there is no published data clearly demonstrating superiority over conventional forms of radiation therapy (external photon beam therapy, electron beam therapy, or brachytherapy) (1).

In order to classify a treatment as "medically necessary", there needs to be clinical evidence that the treatment is effective, has an acceptable toxicity profile, and is better than conventional or standard therapy in terms of outcome, or meaningful side effects and complications.
This document will review the role of PBT in the major cancer sites.

I. Central Nervous System

A. Chondrosarcomas and chordomas of the skull base

These rare primary malignant tumors of the skull base are treated primarily by surgery, and postoperative radiotherapy. There is extensive data on the use of PBT for the treatment of these tumors post-operatively, although there are no randomized trials, and no evidence of the superiority of PBT over conventional therapy in these tumors. While comparison to older historical data of conformal photon radiotherapy may imply some benefit to PBT, more current stereotactic radiosurgery outcomes compare more favorably with PTB results. However, based on the rare nature of these tumors, their location adjacent to critical CNS structures, and the documented efficacy of PTB, treatment of these tumors with PTB will be considered medically necessary.[2-10]

B. Gliomas

Clinical published studies are limited and the results are mixed with one study showing no significant benefit to PBT over conventional treatment, while another small study showed a slightly longer median survival of 20 months, compared to standard photon therapy.[11, 12] At this time there is no data showing significant clinical benefit to PTB in the treatment of gliomas, and this treatment is deemed not medically necessary.

C. Benign CNS tumors

Meningiomas have been treated with PBT with good outcomes, but there is no evidence that this treatment is superior to conventional therapy.[13] Pituitary adenomas have also been treated with PTB[14], but conventional techniques and relatively safe doses of radiation also yield excellent results. PTB is not deemed medically necessary in the treatment of benign CNS tumors.

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II. Ocular Tumors

A. Uveal Melanomas

PBT is effective in the treatment of these tumors with local control rates of over 95%, 85% cause specific survival, and eye preservation rate of 90% (reasonable vision retained in approximately 50%). Intermediate tumors are treated just as effectively with brachytherapy, and the superiority of PBT in these tumors has not been demonstrated. For large uveal melanomas, PBT has been associated with a lower rate of secondary enucleation. Based on the extensive and excellent data on the use of protons in uveal melanomas, PTB is considered medically necessary, particularly in patients who are not optimal candidates for brachytherapy.[15-21]

III. Prostate Cancer

Currently, the evidence does not support any definitive benefit to PBT in the treatment of prostate cancer.[22] IMRT is the most commonly used technique of external beam radiotherapy for the treatment of prostate cancer. There are no published patient-reported outcomes for prostate cancer patients treated with IMRT versus PBT and no prospective studies have been initiated comparing these modalities.

Indeed, there are significant concerns regarding the use of PBT in prostate cancer. The success of PBT depends on the accurate placement of the high dose region of the beam (the Bragg Peak) directly into the tumor. In deep seated mobile targets such as the prostate, where frequent changes to bladder and rectal volumes alter the position of the target, dose can be deposited in normal tissues rather than tumor.

The feasibility of PBT for prostate cancer has been demonstrated going back to the Boston series published in 1979. Studies from the Loma Linda facility have demonstrated that higher doses of protons used a boost treatment are more effective than lower doses of protons, but the same results have been found with conventional external beam radiotherapy. There is no evidence that even higher doses can be delivered with PBT compared to IMRT, without increasing toxicity.

There has been a suggestion that there may be a lower risk of second malignancies with PBT compared to IMRT. A larger volume of normal tissue is exposed low dose radiation with IMRT, and this higher integral dose theoretically could cause a higher rate of second malignancies. However, many Proton facilities in the U.S. use passive scattering PBT, producing secondary neutrons, which may in turn also increase the risk of second malignancies. It is also not clear the significance of these risks in the patient population treated for prostate cancer.

More patients with prostate cancer have been treated with PTB compared to any other cancer site. The outcome is similar to IMRT with no clear advantage from clinical data for either technique in terms of disease control or toxicity. PBT is deemed not medically necessary in the treatment of prostate cancer.[23-30]

IV. Lung Cancer

Radiation therapy is used as a sole modality in the treatment of medically inoperable stage I non-small cell lung cancer (NSCLC). In stage III NSCLC lung cancer radiation therapy is used in conjunction with chemotherapy with or without surgery as definitive treatment. It is also used in limited stage small cell lung cancer (SCLC) with chemotherapy, and in palliative settings.

There is limited data on the use of PBT in lung cancer, and the very significant concern of accurately delivering the high dose Bragg Peak region of protons directly into the target when there is organ motion.

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In stage I lung cancer, recent results of stereotactic radiotherapy (SRS) has yielded excellent control rates of over 90%, with low toxicity in peripheral lesions. While there have been several single institution PBT series, the results are similar to that of SRS. A meta-analysis showed no difference in outcome between SRS and ion therapy. In the case of central tumors within 2 cm of the mediastinum, high toxicity has limited hypofractionated SRS techniques, and theoretically PTB may be beneficial in this setting.

In stage III lung cancer, there are also theoretic advantages to PBT, especially in terms of decreasing toxicity, however, there are currently no published studies describing this.
At this time, PBT for lung cancer is deemed investigational, and not medically necessary in the treatment of lung cancer.[31-39]

V. GI Malignancies

Hepatocellular, esophageal, and pancreatic cancers are treated definitively with radiation therapy, and in these cancers, higher doses to the target, sparing normal tissue, is important. Theoretically, PBT may be useful in these cancers; however, in esophageal and pancreatic tumors there is minimal data on the clinical use of PTB, and therefore PBT remains strictly investigational in these tumors.
In hepatocellular cancer, radiation therapy plays a role in unresectable cancers and in those not amenable to radiofrequency ablation. Stereotactic body radiosurgery (SBRT) has been used, as well as PBT. The larger PBT series are from Japan suggesting excellent local control rates, and modest 2-5 year survival rates. Four retrospective (360 patients) and 2 prospective studies (64 patients) of PBT in patients with hepatocellular cancer show results similar to those achieved with SBRT. In patients with unresectable hepatocellular cancers, who are not optimally treated with radiofrequency ablation or SBRT, PBT will be considered medically necessary.[40-54]

VI. Head and Neck Cancers

IMRT is the conventional form of photon radiation therapy in the treatment of head and neck cancers. The current technique of delivering PBT (passive scattering) has significant limitations in optimally treating head and neck cancers, and even with the potential of intensity modulated PTB, dosimetric uncertainty issues need to be solved. The minimal clinical data on PTB and head and neck cancers makes this treatment investigational.[54-57]

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