
Preface

Primary hepatic tumors, mostly hepatocellular carcinoma (HCC), are the fifth most common cause of cancer-related deaths. Its frequency is progressively increasing worldwide and major investigations are being made in order to improve its dismal prognosis. Similarly, the presence of synchronic or metachronic liver metastases from different tumors (colorectal, neuroendocrine, pancreas, breast, etc.) decreases significantly the probability of survival related with a progressive deterioration in the liver performance. An early detection of the presence of liver tumors (early stages) allows to implement curative therapies, mainly hepatectomy or liver transplantation (for primary tumors), with which 70 % of patients can get a survival of 5 years. However, surgery is suitable in only a minority of them and its selection will depend on the volume and extension of the tumor as well as on the functionality of the remaining liver parenchyma.

For inoperable patients, irrespective of the reason, other therapeutic strategies such as the application of transparietohepatic ablative techniques are actively investigated and, thus, clinically established as effective alternatives, not only to obtain local control of the disease but also to put patients as surgical candidates (downstaging) and then increasing patient's survival. These techniques include radiofrequency, ethanol ablation, microwave ablation, and now, electroporation, and are applicable in both primary and metastatic lesions.

The incorporation, along the past decades, of new drugs for the systemic treatment of metastatic diseases has allowed a dramatic increase in patients' expectations and, for example, in colorectal liver metastases the mean overall survival is four times higher than the obtained with just supportive care (23 mo vs 6 mo). However, if a patient cannot receive surgery his/her life expectancy at 5 years is still as low as 7 %. For this reason, it seems evident that any strategy with which a maximal control of the liver disease can be obtained will have a definitive impact on the survival. Clinical decisions have been oriented toward the combination of drugs with new targeted specific therapies, thus personalizing the strategies to the patients' needs and to combine methods with different, non-summative toxicities that may even multiply their effect. A good example of the latter is the administration of active drugs which are radiosensitizers that may increase the local effect of radiation.

Other possibilities are to increase the local dose by administering the selected agent through the artery that gets the tumor, a branch of the hepatic artery. These trends may be oriented by taking advantage of a unique anatomic characteristic of the liver which is his double blood supply. Since liver neoplasms are mostly (almost exclusive in nodules bigger than 3 mms) supplied by the hepatic artery, any administration from this access may target the tumor and, theoretically, avoid major damage of the healthy, non-tumoral, parenchyma which will be mainly supplied by the portal vein.

The possibility of obtaining an accurate targeting of the liver tumors by an endovascular approach opened in the 1980s a new way to treat patients. Some fundamental investigations have demonstrated that by this approach it is possible to obtain palliation, or to downstage to surgery or, even, to cure by complete ablation, a liver

tumor (mainly HCC). There are many articles, with robust evidence, that have contributed to the allocation of the endovascular procedures in a unique situation within the therapeutic algorithms. This applies mainly for HCC although some liver metastases (i.e., neuroendocrine) have, for years, also been very efficiently treated by this approach.

Focusing on the endovascular treatment of HCC, several articles and reviews have claimed about the great dispersity of procedures that are grouped under the classification of “endovascular treatment.” This may be due to the wide heterogeneity of the underlying disease (different grades of cirrhosis, the presence of hepatitis, etc), some geo-economical issues, and the outstanding creativity of interventional radiologists that push and disperse them, continuously, toward new projects and materials. The consequence is that unfortunately it has been almost impossible, or at least quite difficult, to compare the data obtained from several investigations.

The heterogeneous group of “endovascular procedures” includes bland embolization, chemoembolization and, now, radioembolization. The basic aim of bland embolization is to obtain tumoral necrosis by selectively delivering an occluding material within the afferent arteries thus obtaining ischemia which generates necrosis. Several reports have shown that if the procedure is precisely carried out the tumoral control is very high. Many others have claimed, however, that a “just” bland embolization may, initially, provoke ischemia, but almost immediately, will also trigger the mechanisms of neo-angiogenesis activated by the need of the tumor of new vessels.

This is the reason why in a majority of countries “embolization” has been changed to “chemoembolization,” which means that an active agent (a drug) has been added to the material of embolization. It obviously has increased the heterogeneity of the series making it even more difficult to compare their results.

However, the term “chemoembolization” has introduced a new concept. This concept is that the material for embolization (a fluid as is “Lipiodol” or the particle itself) can be both a carrier and an occluding embolizer. There have been several articles that have shown the advantage of applying occluding particles which deliver drug to the surrounding tissues with marked increases in the local control and in downstaging and final overall survival. Some investigators, however, still claim that the size and amount of the spheres and its intravascular point of delivery, as well as patients’ characteristics, are still too inhomogeneous making it difficult to obtain a final guidance for daily clinical decisions.

The evolving concept is that the particles may just be carriers, avoiding any triggering of neo-angiogenesis and just delivering an active antitumoral agent within the lesion. This initiative has taken profit from the previous knowledge about tumoral characteristics such as anatomy or tumoral hemodynamics and materials for performing the procedure. Nonetheless, it has opened new horizons in terms of delivering new agents to treat tumors. There has always been controversy about the efficacy of chemotherapeutic drugs (as could be for Doxorubicin in HCC) in tumors that have constantly demonstrated its chemoresistance and, for this reason, several groups have, for years, been working on new possibilities for materials that may be delivered locally killing the tumoral cells in different, sometimes, very sophisticated ways. Among them are gene therapy, targeted therapies, hyperthermia, or radiation. The latter is termed as Radioembolization (RE) or, in some places, Selective Internal Radiation Therapy; both terms define the concept of the procedure and the former states that radiation is administered with the aid of an endovascular carrier (embolizer).

The evolving therapeutic strategies raise continuously new challenges. It seems evident that the methodology that needs to be applied for each precise endovascular procedure should/must be different from one another. It is not just the matter of making an angiography and placing selectively a microcatheter and then a bland, or a chemo or a radioembolization can be consecutively performed. Every procedure has its specific requirements. Similarly, the criteria of selection and the methods to evaluate response

may be different. Nowadays, for example, the excellent RECIST classification has been surpassed for some specific treatments such as targeted therapies or endovascular treatments, among them RE.

The term RE refers to the administration of brachytherapy with microspheres embedded with a beta-emitting isotope (Yttrium-90). RE was initially performed in the 1990s and mainly in Australasia; it was later approved in the USA and initiated in Europe in 2003. Currently, many institutions worldwide are using RE, alone or in combination with other treatments, as a fully established modality to treat patients with primary and metastatic liver malignancies. RE has already proven its efficacy in different tumoral indications and seems to be unique in terms of comparison of results. Since the performance of the procedure requires an accurate knowledge of the precise tumoral, and non-tumoral, volume that is going to be treated, since the exact dose that has been administered is precisely detailed, and since the clinical situation must be carefully scrutinized, it is easier to show exactly what is being done to each patient regardless of the institution in which he is being treated. This unique characteristic is offering an easier understanding of its results in different tumoral situations allowing to know the expectancies that can be obtained in many subgroups of patients.

As in many other therapeutic initiatives, the implementation of RE requires some local regulations and a multidisciplinary approach where specialists from different fields (Medical Oncology, Surgery, Hepatology, Nuclear Medicine, Radiology and Radiation Oncology) give their expertise and knowledge with the aim of increasing its accuracy and efficacy and, at the same time, decreasing its possible morbidity. The book has been structured and organized in order to obtain, from experts in such a multidisciplinary approach, an overview of the most important items related to RE. The chapters deal with the selection of the most adequate candidates, their careful evaluation, the work-up needed to administer the microspheres directly to the tumor, and the results obtained in patients affected from primary and a different range of metastatic liver malignancies.

There are, at this moment, a large number of papers that give robust information related to the fundamental aspects of RE. New fresh information will appear in the following years trying to answer to crucial questions that, obligatorily, are continuously appearing about the procedure itself and about its continuous adaptation to the specific needs of each patient and may be of new tumoral locations.

We thought that there is a need, at this moment, to summarize and discuss in a book all matters related with RE. With this book readers will find the basic and advanced information needed not only to be familiar with but also to incorporate RE in their clinical activity.

José Ignacio Bilbao

Liver Radioembolization with 90Y Microspheres

Bilbao, J.I.; Reiser, M.F. (Eds.)

2014, XIII, 188 p. 125 illus., 25 illus. in color., Hardcover

ISBN: 978-3-642-36472-3