Development of a Database for Storage and Analysis of Factors Affecting Treatment of Hepatocellular Carcinoma

A Thesis submitted to The University of Arizona College of Medicine-Phoenix in partial fulfillment of the requirements for the Degree of Doctor of Medicine

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Abstract

Hepatocellular carcinoma (HCC) is the fifth most common solid tumor worldwide. There are 626,000 new cases per year of primary liver cancer worldwide, most of which are HCC. Over 1,000,000 people die of HCC per year, making HCC the third most frequent cause of cancer deaths worldwide[1]. Major etiologic factors associated with HCC include chronic HBV and HCV infection, chronic alcoholism, non-alcoholic steatohepatitis, and aflatoxin exposure. The standard treatment for HCC is surgical resection, however on presentation many patients have progressed to the point where such treatment is not an option, and are placed on liver transplant lists. Palliative treatment modalities are often used in the interim, including trans-arterial chemoembolization (TACE), radiofrequency ablation (RFA), or systemic chemotherapy. In this study over 200 patients who received either Therasphere or Sirsphere (TACE methods), or RFA treatment for unresectable HCC were catalogued in a relational database allowing for analysis of treatment outcomes and treatment comparisons. A Microsoft Access database was created to store data such as patient demographics, disease details, adverse events, patient lab values, treatment details, and pre- and post-lesion measurements. This database is currently in use by the department of Interventional Radiology at Banner Good Samaritan Medical Center.

Table of Contents

List of Figures and Tables

Introduction

HCC Overview: epidemiology, etiology, and disease course

Hepatocellular carcinoma (HCC) is the third most common cause of cancer deaths worldwide, with over a million deaths per year globally and approximately 12,000 deaths in the United States yearly[1]. HCC is more common in men with a ratio of 2.4:1. It is the most common of the primary liver cancers and has a significantly increased incidence in Southeast Asia and Africa (Fig. 1).

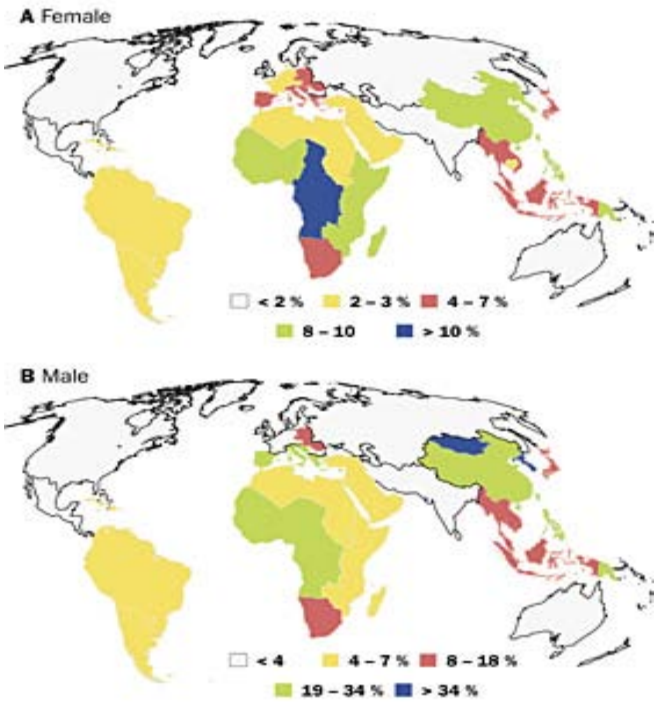


Figure 1. Geographic distribution of hepatocellular carcinoma incidence rates (%) in total population A, female; B, male. Reprinted from Johns Hopkins Gastroenterology and Hepatology website:

(http://www.hopkinsgi.org/GDL_Disease.aspx?CurrentUDV=31&GDL_Cat_ID=024CC2E1-2AEB-4D50-9E02-C79825C9F9BF&GDL_Disease_ID=A349F0EC-5C87-4A52-9F2E-69AFDB80C3D1)

These areas may have endemic rates of HBV infection, which as will be discussed, is a major etiologic factor for the development of HCC. In the United States, HCC incidence has increased by 25% between 1993 and 1998, due not only to chronic HBV and HCV infection but also to alcoholic cirrhosis.

In developing nations, the most common etiologic factors are chronic HBV infection, and aflatoxin exposure. HBV is transmitted parenterally, and in endemic regions is commonly passed by vertical transmission from mother to infant. This form of transmission confers a 200 fold increased risk for HCC development by adulthood (most commonly between 20-40 years of age)[2]. Vaccination projects have great potential in these areas, for example a program begun in Taiwan in 1984 reduced the rates of HBV infection from 10% to 1% in 20 years[3]. Also in these regions aflatoxin exposure appears to confer a major risk for development of HCC. Aflatoxin is produced by *Aspergillus flavus*, a common contaminant in peanuts and some grains. Aflatoxin is known to bind covalently with DNA and cause a mutation in p53, a tumor suppressor protein. In developed countries chronic viral infection (HBV or HCV), chronic alcoholism, and non-alcoholic steatohepatitis are the most common etiologic factors for HCC. Rarer risk factors for the development of HCC include tyrosinemia, genetic hemochromatosis, glycogen storage diseases, and α1-antitrypsin deficiency[4]. Of these, tyrosinemia is most likely to give rise to HCC,

with 40% of tyrosinemic patients developing HCC despite adequate dietary control. In developed countries cirrhosis is present in 75-90% of HCC cases.

The molecular mechanisms by which HCC arises has not been fully elucidated, and are clearly different for different instigating events. As with any cancer, a genetic mutation or mutations are introduced that causes the cell to replicate at a higher rate and/or results in the cell avoiding apoptosis. It is believed that infection by HBV (a DNA virus) causes integration of the viral genome to the host genome, potentially causing the expression of protooncogenes[5]. HCV is an RNA virus, and it is believed that infection by this virus causes repeated cycles of cell death and regeneration resulting in accumulation of mutations at every cycle[6].

Although most HCCs appear to arise from viral insult or a cirrhotic picture, a small subgroup of these tumors express genes present in fetal liver and liver progenitor cells, suggesting that some HCCs may arise from liver stem cells[7].

Screening, Diagnosis, Clinical presentation and Disease course

Screening is recommended for high risk patients. For example, in HBV-endemic areas some HBV carriers are recommended to be screened every 6-12 months irrespective of presence of cirrhosis. This screening frequency is based on the doubling time of HCC[8]. Screening is recommended for chronic HBV carriers; men over the age of 40 years and women over the age of 50 years. Other groups for whom screening is recommended are those with a family history of HCC, those with

non-HBV cirrhosis such as HCV, alcoholic, hemochromatosis, primary biliary cirrhosis, non-alcoholic steatohepatitis, autoimmune heptatitis, and patients with α1-antitrypsin deficiency.

Alpha-fetoprotein (AFP) and abdominal ultrasound are the most commonly used screening methods, however these must be used in conjunction as alpha-fetoprotein has a low sensitivity for HCC[9]. Elevated serum alpha fetoprotein levels are found in 50% of people with HCC, but false positives may occur in patients with yolk-sac tumors, cirrhosis, chronic hepatitis, normal pregnancy, fetal distress or death, and fetal neural tube defects such as anencephaly or spina bifida. AFP at high levels (above 200 ng/ml) is highly specific for HCC in patients with cirrhosis and coinciding radiologic evidence of hepatic lesions[10].

The most reliable diagnostic tests for HCC are triple-phase helical CT and triple-phase dynamic contrast MRI[11]. The characteristic pattern on these scans for HCC is the presence of arterial enhancement followed by delayed hypointensity of the tumor in the portal venous and delayed phases (washout) (Fig. 2). Diagnosis can be established by imaging alone if a focal hepatic mass greater than 2 cm is identified with characteristic contrast enhancement features on the arterial phase with venous washout on an MRI or CT. With unclear imaging findings on CT/MRI, diagnosis can be established by a biopsy of the lesion, although this is less desirable as tumor cells may be tracked out from the path of the biopsy needle.

Currently, research is being conducted to identify molecular signatures of HCC to assist in detection of very early stage HCC[12].

Without intervention, the natural course of HCC leads to progressive enlargement of the primary mass until it seriously disturbs hepatic function or metastasizes, first generally to lungs and then to other sites.

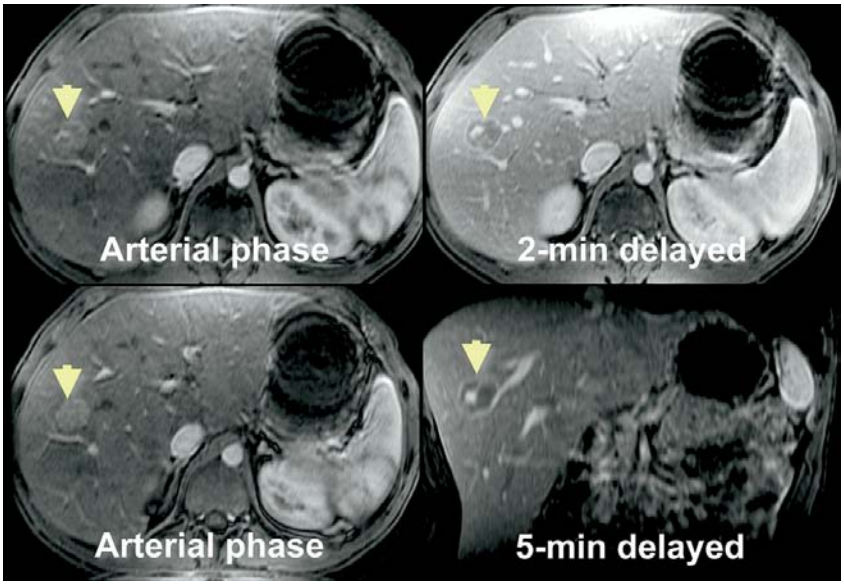


Figure 2. MRI features of HCC showing arterial phase enhancement (top and bottom left) followed by hypointense signals on the venous face (top and bottom right).

Following hepatic disruption (via invasion or occlusion of the portal vein or IVC) or metastasis, death usually occurs from cachexia, GI or esophageal bleeding, liver failure with hepatic encephalopathy/coma, or rarely, rupture of the tumor with fatal intraabdominal hemorrhage. At any stage, the patient with HCC may present with right upper quadrant pain, malaise, fatigue, weight loss, and/or worsening liver function tests. If the patient is cirrhotic, signs and symptoms of cirrhosis may also be present, including jaundice, portal hypertension

manifesting in ascites and varices, palmar erythema, and/or gynecomastia.

HCC may exist as a unifocal mass, multifocal masses of variable size, or as a diffusely infiltrative tumor. All patterns have a strong propensity for invasion of vascular structures.

HCC Staging

To determine the best treatment for patients presenting at different points in disease progression, several staging systems have been proposed, although no one system is universally accepted. For this project, the Child-Pugh system, which provides as assessment of synthetic function and Okuda, which takes into account radiologic tumor size and liver function (ascites, total serum bilirubin, and serum albumin) were utilized[13].

Very early stage HCC (with a single nodule < 2 cm) is difficult to diagnose, and when found, is usually found incidentally. For such early stage HCC, resection and radiofrequency ablation (RFA, discussed below) likely offer similar 2 year survival rates[14].

Early stage HCC is defined as a solitary node or up to 3 nodules each less than or equal to 3 cm. The 5 year survival rate in these patients following treatment with surgical resection, liver transplant, or RFA is up to 75%.

Intermediate stage HCC presents with cirrhosis but without vascular invasion. For these patients, transarterial chemoembolization (TACE, discussed below) leads to a 23% improvement in 2 year survival compared with conservative therapy.

In patients who are classified as having advanced stage HCC, TACE may increase survival. Sorafenib is a relatively new treatment which is a tyrosine protein kinase inhibitor and is approved for treatment of advanced stage HCC. Sorafenib increases survival compared with placebo and is the best treatment option for patients in the advanced stage of HCC[15].

Patients in the terminal stage of HCC present with progressive liver failure as described above to the point of physical impairment. These patients have a 1 year survival rate of less than 10%.

HCC Treatment

Several treatment options exist for patients with HCC, however not all treatments are helpful to all patients. Surgical resection offers the best prognosis, but only 10-15% of patients are candidates as a result of extensive disease or poor liver function. In a liver damaged by cirrhosis, 40% of the liver must be able to be retained following surgical resection for the patient to have enough residual function after surgery. In non-cirrhotic livers, the remnant must be greater than 25% of the original size in order to ensure adequate residual function. Surgical resection thus offers the greatest benefit for patients with small tumors, absence of vascular invasion, and preserved liver function.

Liver transplant also an excellent treatment in the right candidate. Transplant patients with non-metastatic HCC have excellent long-term survival. Recent restructuring of transplant candidate criteria by the United Network for Organ Sharing (UNOS) have improved the 5

year survival rates post-transplant to >70% and recurrence rates to <15% [16].

In patients who are not eligible for resection or transplantation, minimally invasive percutaneous methods are ideal treatments. Radiofrequency ablation (RFA, Fig.3) uses high frequency alternating current to elevate the temperature at the point of interest to the point where permanent tissue damage is caused. In the case of HCC, a probe is passed transcutaneously and placed near the tumor to cause local tissue destruction. RFA has proved to be a good treatment for tumors < 5 cm. A randomized controlled clinical trial showing outcomes of surgical resection of HCC vs. RFA showed similar survival rates at 4 years and less morbidity for patients treated with RFA[17].

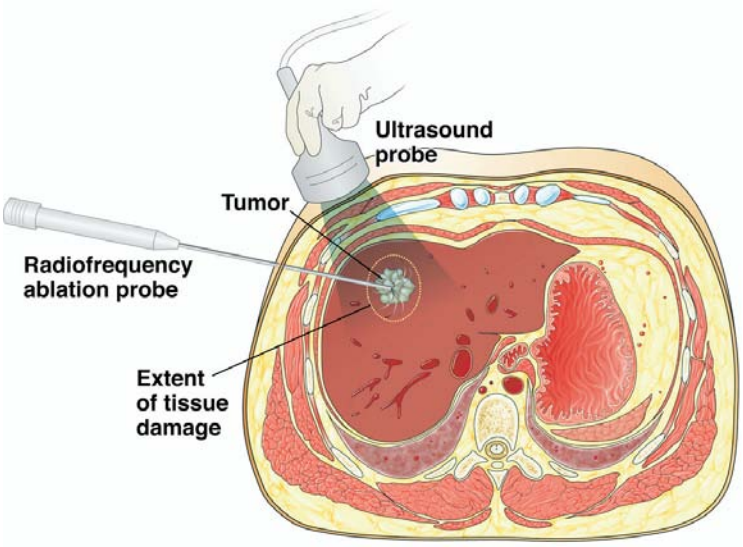


Figure 3. Radiofrequency ablation of HCC.

Transarterial chemoembolization (TACE) is a technique used to directly target the region(s) of the liver containing the HCC. Access to

the proper hepatic artery is gained by passing a catheter from the common femoral artery, cephalad through the abdominal aorta, into the celiac trunk and common hepatic artery into the proper hepatic artery. To place the catheter tip as close as possible to the region of involvement, an arteriogram is done prior to advancing the catheter tip through minor vessels closer to the tumor. At this point the vessel may be embolized and/or injected with combined embolic and chemotherapeutic particles[18]. These particles may be glass (Theraspheres) or resin (SIR-spheres) coated with the radioactive element Yttrium 90 (where the technique is termed transarterial radio-embolization) or combined with a chemotherapeutic agent such as doxorubicin, mitomycin, or cisplatin. TACE may offer palliative benefits for patients with intermediate stage HCC, resulting in 5 year survival rates after treatment exceeding 50%[19]. In a large prospective cohort study of 8510 pts who received TACE for unresectable HCC, the median survival was 34 months with 1, 2, 3, 5, and 7 year survivals of 82%, 47%, 26%, and 16% [20]. Although TACE is a proven effective treatment of HCC, there is little data to guide the choice of chemotherapy or the number of treatments to schedule. Adverse events may also occur with TACE, including ischemic cholecystitis, nausea, bone marrow depression, and abdominal pain in up to 10% of treated patients[21]. Additionally, a post-embolization syndrome has been described in more than 50% of patients which includes fever, abdominal pain, and moderate intestinal obstruction. The mortality rate for TACE treatment is less than 5%. Currently, TACE is the first-line treatment for patients in intermediate disease stages who exceed

the criteria for liver transplantation. It is also an alternative to RFA in patients who have tumors in inaccessible locations to an RFA probe. Lastly, TACE and RFA may be used to downstage a tumor so that a patient who does not meet criteria for resection or transplant may become eligible for those treatments. Studies have shown that successful tumor downstaging can be achieved in up to 70% of the patients treated with TACE, RFA, or percutaneous ethanol injection and that successful transplant was achieved in 50% of these patients[22].

HCC Database

Although Banner Good Samaritan Medical Center is a leading institution in the treatment of hepatocellular carcinoma, no database for tracking patient response to treatments existed until this project was completed. With the high volume of patients with HCC and the various treatment modalities available, this database addresses a critical need for retrospective analysis of patient treatment outcomes.

As will be described in following sections, many patient variables pertinent to HCC are collected in this database. Patient demographics, such as race, sex, age, diagnosis date, current status (living or deceased), days of survival, number of interventional radiology treatments, treatment type(s), disease etiology, lesion distribution and morphology, characteristics of the disease such as presence of ascites, portal vein thrombosis, etc, as well as standard prognostic scores including Okuda, Child-Pugh and ECOG are listed. Lab values, including α-fetoprotein levels, AST, ALT, alkaline phosphatase, albumin, total bilirubin, PT and INR are stored for each

patient. Pre- and post-treatment lesion measures and degree of necrosis are listed for each tumor in each patient. Treatment details including radiation dose date, dose, and region of distribution are also stored in the database.

A user-friendly entry form has been created for the entry of all of this information, however a future goal might be to extract all pertinent data from the EMR and automatically populate the HCC database. Although this could potentially save some effort, data which are stored in physician notes such as lesion measurements, treatment details, and disease etiology would still likely need to be entered manually.

Research Materials and Methods

The initial set of data for this project was collected by hand by Dr. David Wood and compiled by members of the Interventional Radiology department in a Microsoft Excel file. This method of data entry was cumbersome and it was very difficult to produce reports for a particular patient or particular set of variables. The original data was extracted manually from patient medical records, from records in the BGS liver center, and from observations made during IR procedures.

To create the Access database, data which fit well together in groups (such as patient demographics or patient lab values) were placed in tables together. The first table was titled "pt_demo_dz_descript_ad_events," and was created in Design View (Fig. 4).

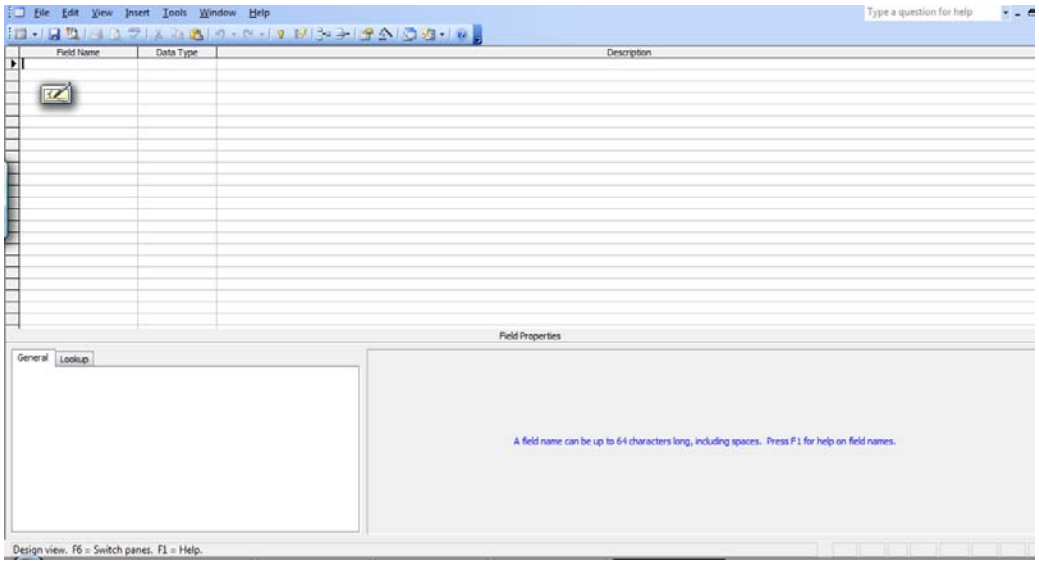
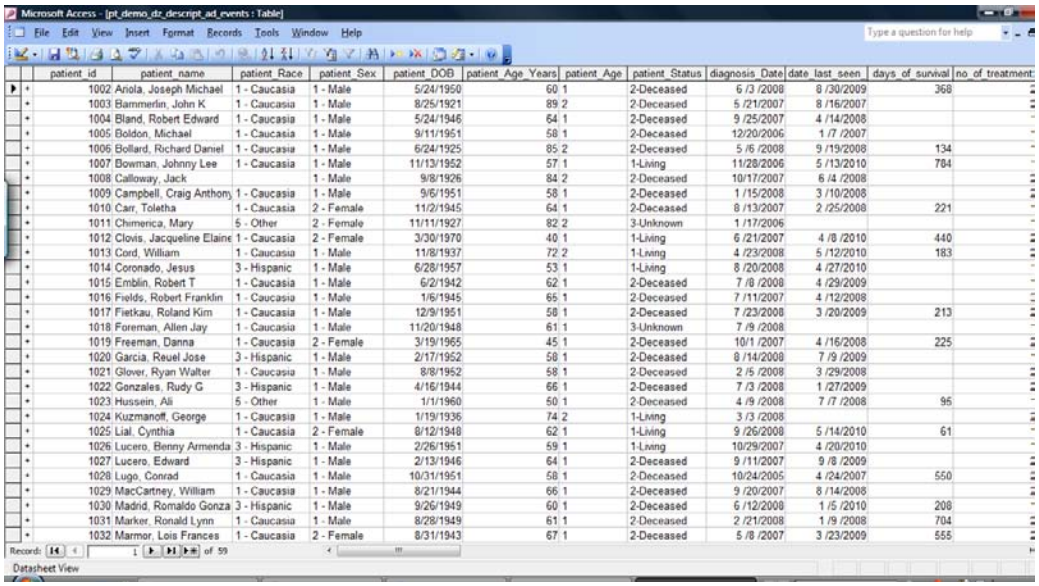


Figure 4. Construction of table "pt_demo_dz_descript_ad_events" in design view.

The field included a patient ID field, which was a unique number assigned to each patient. This table also contained fields for patient name, race, sex, date of birth, age, status (living or deceased), diagnosis date, date last seen or date of death, and days of survival. Fields pertaining to the general treatment received such as disease etiology, number of lesions, lesion distribution (bilobal, multilobal, etc), lesion morphology (uninodular, multinodular, diffuse), percent replacement of the liver by tumor, macroscopic vascular invasion, and extrahepatic spread were also included. Fields pertaining to the signs and symptoms of disease were added including portal hypertension, portal vein thrombosis, lymphadenopathy, ascites, HCV or HBV infection, and encephalopathy were also included in this table. Fields for entry of prognostic scores such as Child-Pugh, Okuda, and ECOG were also added to this table. Lastly, fields for entry of adverse events

including increased alkaline phosphatase, total bilirubin, AST, and ALT and presence of fever, chills, abdominal pain, and fatigue were included on this table (Fig. 5)



Microsoft Access - [pt_demo_dz_descript_ad_events : Table]

File Edit View Insert Format Records Tools Window Help

patient_id	patient_name	patient_Race	patient_Sex	patient_DOB	patient_Age_Years	patient_Age	patient_Status	diagnosis_Date	date_last_seen	days_of_survival	no_of_treatment
1002	Ariola, Joseph Michael	1 - Caucasia	1 - Male	5/24/1950	60	1	2-Deceased	6 /3 /2008	8 /30/2009	368	
1003	Bammerlin, John K	1 - Caucasia	1 - Male	8/25/1921	89	2	2-Deceased	5 /21/2007	8 /16/2007		
1004	Bland, Robert Edward	1 - Caucasia	1 - Male	5/24/1946	64	1	2-Deceased	9 /25/2007	4 /14/2008		
1005	Boldon, Michael	1 - Caucasia	1 - Male	9/11/1951	58	1	2-Deceased	12/20/2006	1 /7 /2007		
1006	Bollard, Richard Daniel	1 - Caucasia	1 - Male	6/24/1925	85	2	2-Deceased	5 /6 /2008	9 /19/2008	134	
1007	Bowman, Johnny Lee	1 - Caucasia	1 - Male	11/13/1952	57	1	1-Living	11/28/2006	5 /13/2010	784	
1008	Calloway, Jack		1 - Male	9/8/1926	84	2	2-Deceased	10/17/2007	6 /4 /2008		
1009	Campbell, Craig Anthony	1 - Caucasia	1 - Male	9/6/1951	58	1	2-Deceased	1 /15/2008	3 /10/2008		
1010	Carr, Toletha	1 - Caucasia	2 - Female	11/2/1945	64	1	2-Deceased	8 /13/2007	2 /25/2008	221	
1011	Chimerica, Mary	5 - Other	2 - Female	11/11/1927	82	2	3-Unknown	1 /17/2006			
1012	Clovis, Jacqueline Elaine	1 - Caucasia	2 - Female	3/30/1970	40	1	1-Living	6 /21/2007	4 /8 /2010	440	
1013	Cord, William	1 - Caucasia	1 - Male	11/8/1937	72	2	1-Living	4 /23/2008	5 /12/2010	183	
1014	Coronado, Jesus	3 - Hispanic	1 - Male	6/28/1957	53	1	1-Living	8 /20/2008	4 /27/2010		
1015	Emblin, Robert T	1 - Caucasia	1 - Male	6/2/1942	62	1	2-Deceased	7 /8 /2008	4 /29/2009		
1016	Fields, Robert Franklin	1 - Caucasia	1 - Male	1/6/1945	65	1	2-Deceased	7 /11/2007	4 /12/2008		
1017	Fietkau, Roland Kim	1 - Caucasia	1 - Male	12/9/1951	58	1	2-Deceased	7 /23/2008	3 /20/2009	213	
1018	Foreman, Allen Jay	1 - Caucasia	1 - Male	11/20/1948	61	1	3-Unknown	7 /9 /2008			
1019	Freeman, Danna	1 - Caucasia	2 - Female	3/19/1965	45	1	2-Deceased	10/1 /2007	4 /16/2008	225	
1020	Garcia, Reuel Jose	3 - Hispanic	1 - Male	2/17/1952	58	1	2-Deceased	8 /14/2008	7 /9 /2009		
1021	Glover, Ryan Walter	1 - Caucasia	1 - Male	8/8/1952	58	1	2-Deceased	2 /5 /2008	3 /29/2008		
1022	Gonzales, Rudy G	3 - Hispanic	1 - Male	4/16/1944	66	1	2-Deceased	7 /3 /2008	1 /27/2009		
1023	Hussein, Ali	5 - Other	1 - Male	1/1/1960	50	1	2-Deceased	4 /9 /2008	7 /7 /2008	95	
1024	Kuzmanoff, George	1 - Caucasia	1 - Male	1/19/1936	74	2	1-Living	3 /3 /2008			
1025	Lial, Cynthia	1 - Caucasia	2 - Female	8/12/1948	62	1	1-Living	9 /26/2008	5 /14/2010	61	
1026	Lucero, Benny Armenda	3 - Hispanic	1 - Male	2/26/1951	59	1	1-Living	10/29/2007	4 /20/2010		
1027	Lucero, Edward	3 - Hispanic	1 - Male	2/13/1946	64	1	2-Deceased	9 /11/2007	9 /8 /2009		
1028	Lugo, Conrad	1 - Caucasia	1 - Male	10/31/1951	58	1	2-Deceased	10/24/2005	4 /24/2007	550	
1029	MacCartney, William	1 - Caucasia	1 - Male	8/21/1944	66	1	2-Deceased	9 /20/2007	8 /14/2008		
1030	Madrid, Romaldo Gonza	3 - Hispanic	1 - Male	9/26/1949	60	1	2-Deceased	6 /12/2008	1 /5 /2010	208	
1031	Marker, Ronald Lynn	1 - Caucasia	1 - Male	8/28/1949	61	1	2-Deceased	2 /21/2008	1 /9 /2008	704	
1032	Marmor, Lois Frances	1 - Caucasia	2 - Female	8/31/1943	67	1	2-Deceased	5 /8 /2007	3 /23/2009	555	

Record: 1 of 59

Datasheet View

Figure 5. pt_demo_dz_description_ad_events table

A form titled "Patient and Disease" was then created to enable user access to the data in the tables. This form was created in Design View using combo boxes, list boxes, and command buttons to allow data entry to proceed via dropdown menus. For fields with multiple potential values, a particular value could be chosen from the drop down menu (Fig. 6) and for binary values a "yes" or "no" choice could be selected from a drop down menu (Fig. 7).

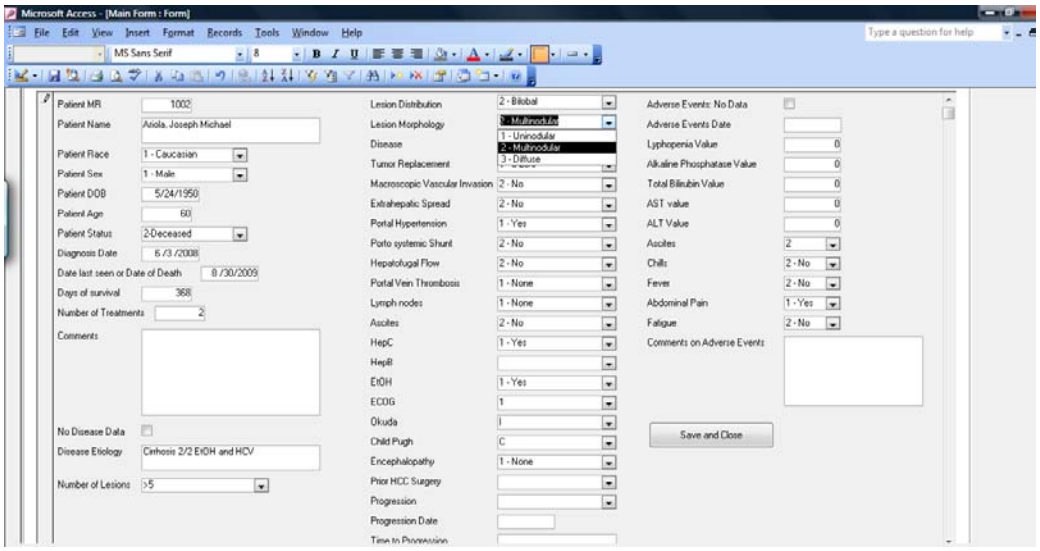


Figure 6. Drop down multiple choice boxes in patient data entry form

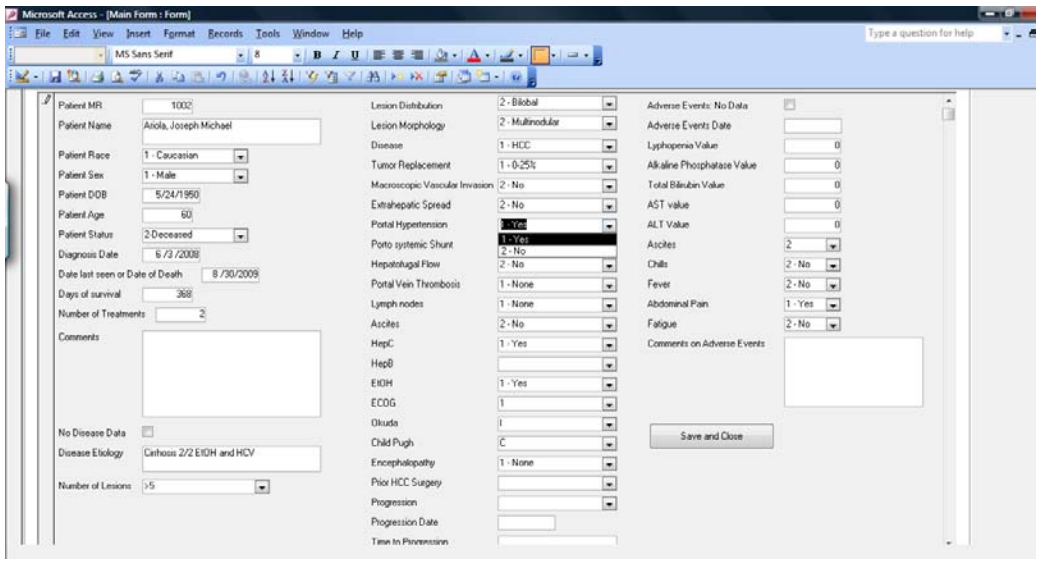


Figure 7. Drop down binary yes/no boxes in patient data entry form

The next table for data storage details was called "treatment_details" and included the following fields: patient ID, treatment ID (first, second, or third treatment), description (segmental,right or left lobe,

etc.), treatment type, dose date, dose (Gy), volume of thera or sir-spheres, fraction of liver treated, whole liver volume, total lung dose in mci and total lung dose in Gy. A comments field was also added to this table (and to all tables) to allow for any information to be entered as free text which was not accounted for in the table fields. Additionally, a "no data" check box was included in all forms to allow for indication that data was not collected for this patient. A form for data entry and display corresponding to the treatment_details table also titled "Treatment Details" was constructed (Fig. 8)

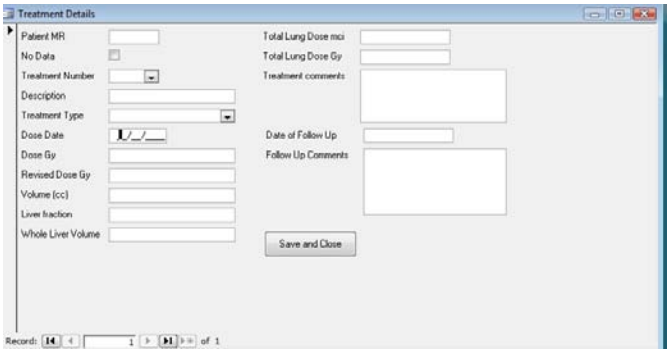


Figure 8. Treatment details form

All fields in this form are free text except for the date field, where dashes separate day/month/year, and for the treatment number and treatment type fields, for which drop down menus were created. A command button "save and close" allows data entered to be stored in the corresponding table. Data stored in the treatment_details table can be viewed in form view by tabbing through the records at the bottom of the form.

A third table, "lesion_measures," contains the following fields: treatment ID, lesion number, date of measurement, measurement of

the lesion in two dimensions (les and ortho measurement), necrosis (greater or less than 50% tumor necrosis), WHO EASL response and a free-text comment field. The corresponding form titled Lesion Measures was constructed (Fig. 9) using drop down menus for the lesion number, degree of necrosis, and WHO EASL response fields and free text for all other fields.

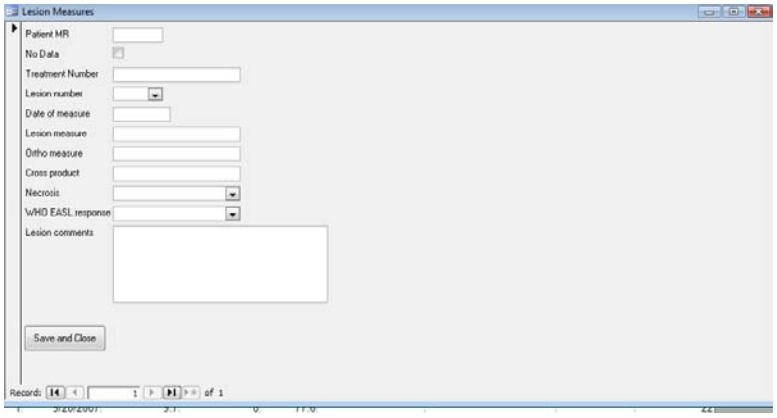


Figure 9. Lesion measures table.

A fourth data table titled "lab_values" was created in design view (as with all tables and forms) with the following fields: patient ID, treatment ID, lab date, AFP value, total bilirubin value, albumin value, AST and ALT values, alkaline phosphatase value, and PT and INR values. With the creation of a lab date field, multiple lab data sets can be stored for a single patient. The corresponding form is titled Lab Values and is displayed in Fig. 10. In this form, the only drop down menu is the treatment number field, which indicates the treatment for which this set of labs was drawn.

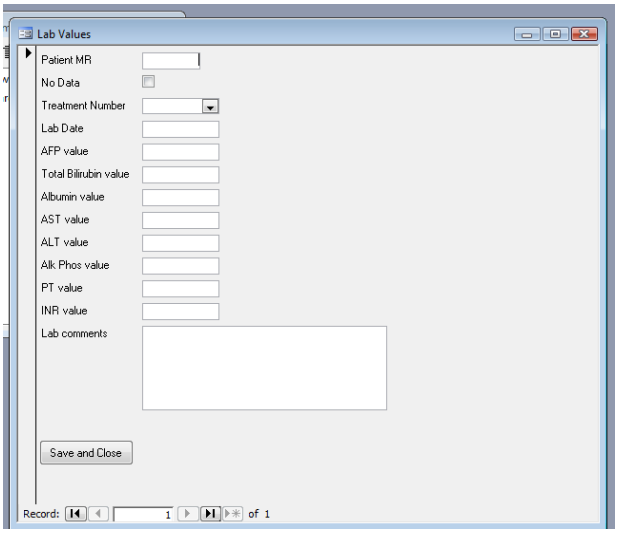


Figure 10. Lab values form.

After all of the tables were formed to store raw data, and corresponding forms were constructed to allow for easy data entry and review, a structure allowing for cohesive data entry was created by the formation of a "Main Switchboard" form which operated off of a table titled "switchboard items." The form was created using the "Tools" dropdown menu in the main Access screen, selecting "database utilities," then "switchboard manager" and selecting "edit." (Fig. 11)

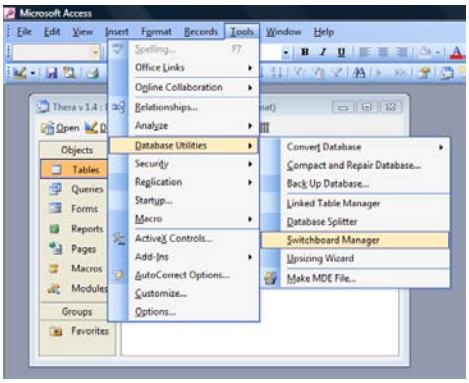


Figure 11. Creation of Main Switchboard

From this point, and "edit switchboard page" box was used to enter items wished to be included on the switchboard. The items created were "Enter patient data" to allow for easy data entry, "View patient reports" to quickly view reports on a particular patient or set of patients, and "exit" to exit the switchboard (Fig. 12)

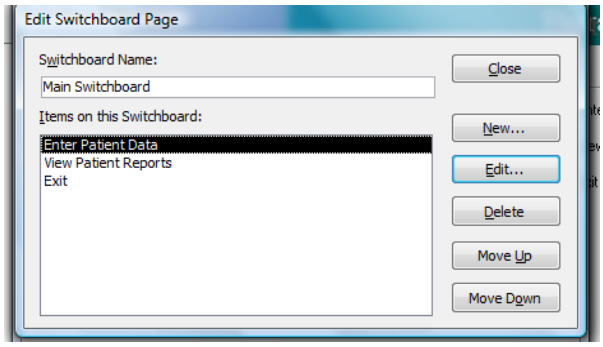


Figure 12. Creation of Main Switchboard (continued).

Each entry was highlighted and the "edit" option was chosen (Fig. 13) which allowed for the text to be displayed ("enter patient data," "view patient reports," and "exit."). A command field allowed the desired command to be chosen, for example, when selecting the "enter patient data" option, the command chosen was to "open form in add mode."

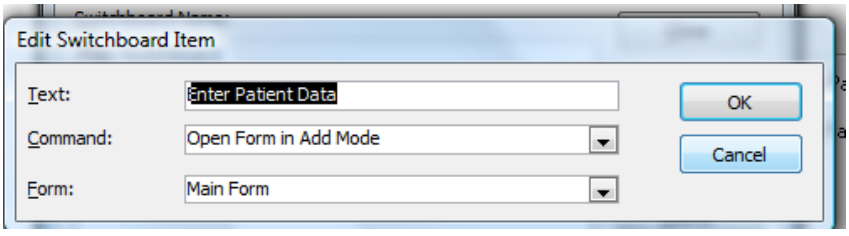


Figure 13. Creation of Main Switchboard (continued).

Finally, The Form field allowed for selection of the form to which data would be added or viewed, for example the Main Form which is a form combining the Patient and Disease form, Treatment details form, Lesion measure form, and lab values form in tabbed format. In the case of creating reports, the item on the switchboard was "view patient reports," the command chosen was "Open form in add mode," and the form chosen was the "Report builder" form. The finalized switchboard manager appeared as shown in Fig. 14. This screen comes up upon initialization of the database, so that the user can immediately choose to enter new patient data, create a report for a single patient or multiple patients, or exit the program.

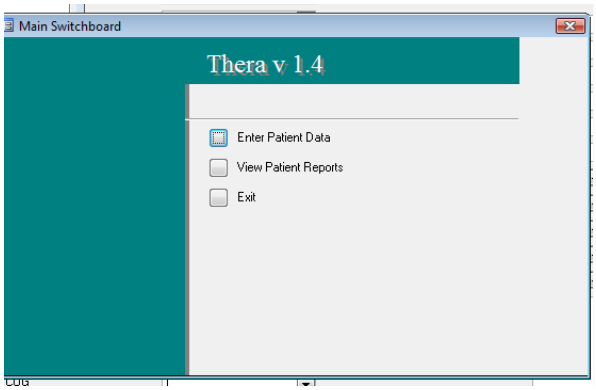


Figure 14. HCC database Main Switchboard screen

Choosing "Enter patient data" from this screen opens the main form which appears as shown in Fig. 15. The four minor forms are accessible by tabs from the single main form.

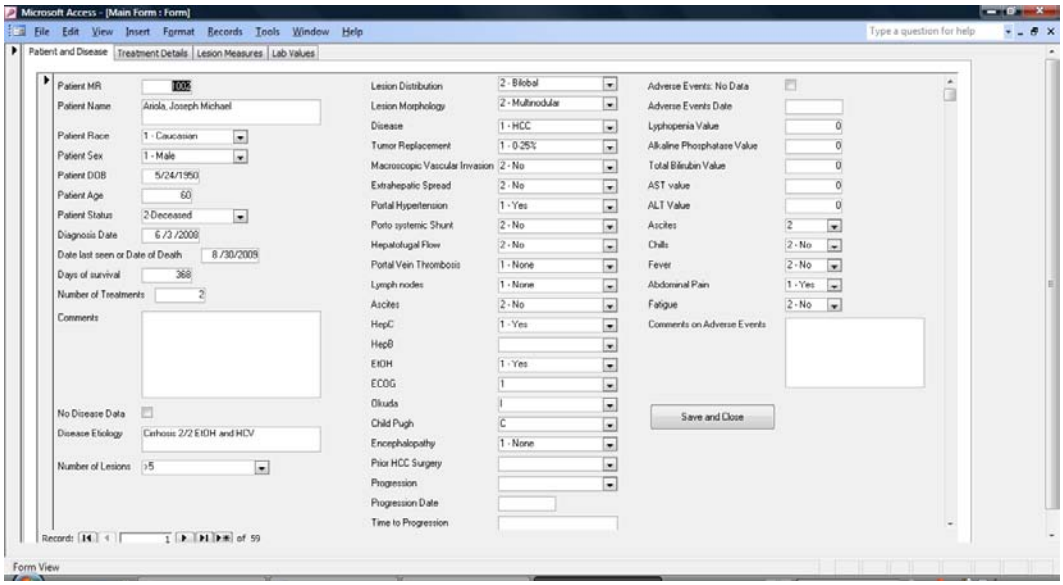


Figure 15. HCC database Main data entry form with tabs

Queries

The HCC database at this point had the ability to store large amount of information for each patient and with the switchboard allowed easy and intuitive data entry. The next step was to create a set of queries to extract desired data. This was accomplished using the query wizard option (Fig. 16). Using this wizard, desired fields from tables of interest could be selected for data extraction by the query by moving items from the "available fields" section to the "selected fields" section. The next screen gave two options, the "Detail" option which allows, for example, all lab values to be pulled for a single patient, or the "Summary" option, which allows for all patients with a certain lab value to be pulled.

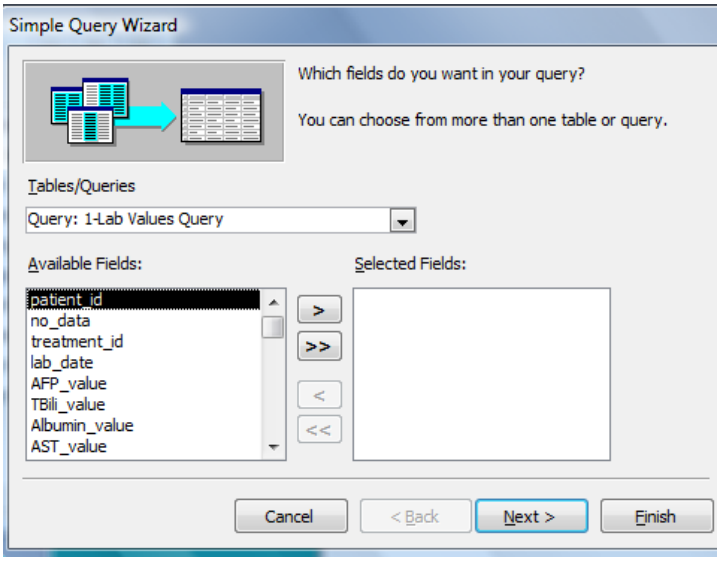


Figure 16. Creation of Query with Query wizard.

Each query was given a name (Lab values query, lesion measure query, pt demographics query, adverse events query, and treat_lesion_lab query). Although all information extracted by the query could be pulled up simply by selecting "queries" on the main navigation panel (Figs. 17 and 18), the most user-friendly form of data presentation is to create a report, which is described in the next section.

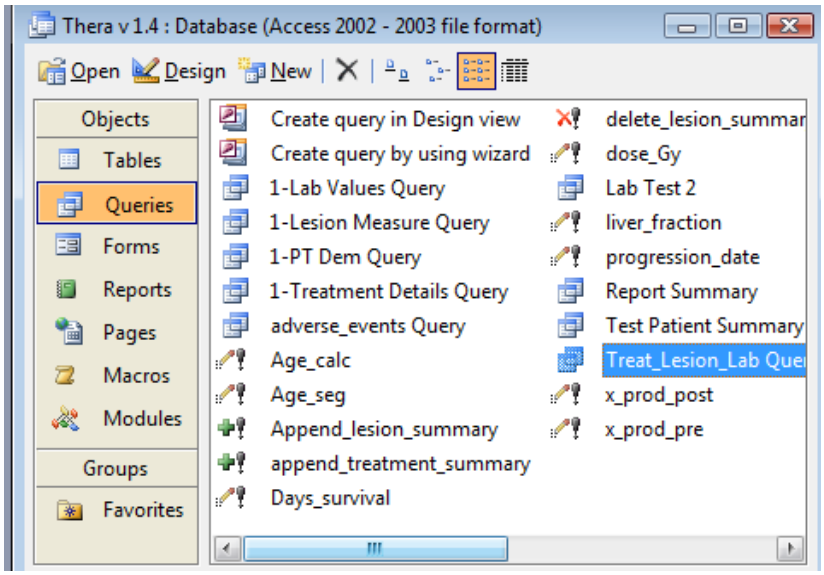


Figure 17. Selection of a query to be run from the MS Access console

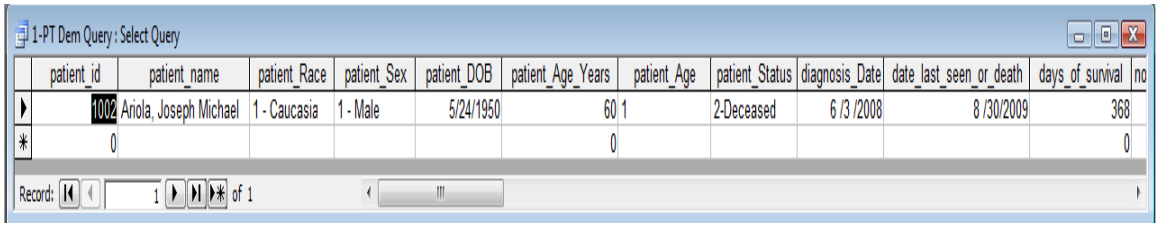


Figure 18. Results of a query run from the MS Access console, in table form.

Reports

Reports are compilations of data drawn from tables by a query. Data is presented in an easy to read format and in whatever structure the query dictates. For this project, reports were created using the report wizard. Fields desired to be displayed on a report were chosen in the first step (Fig. 19).

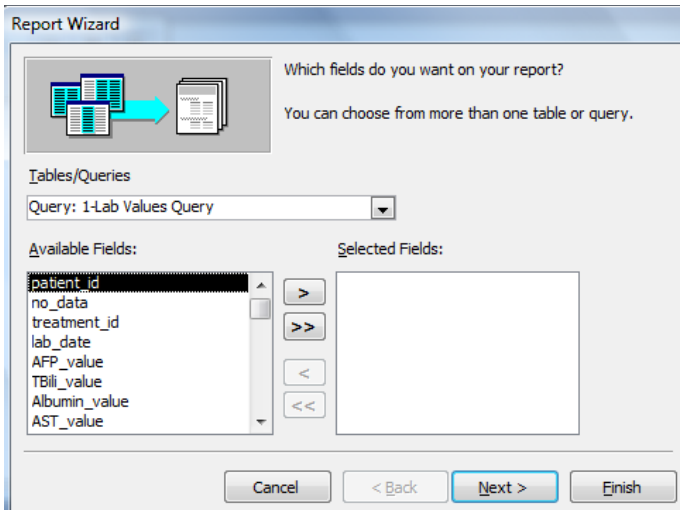


Figure 19. Choosing fields to be included in a report.

The next step is to choose a grouping level, or a piece of data which ties all other pieces of data together. The most obvious choice for this was the patient ID (Fig. 20) which would carry with it all associated data for a particular patient.

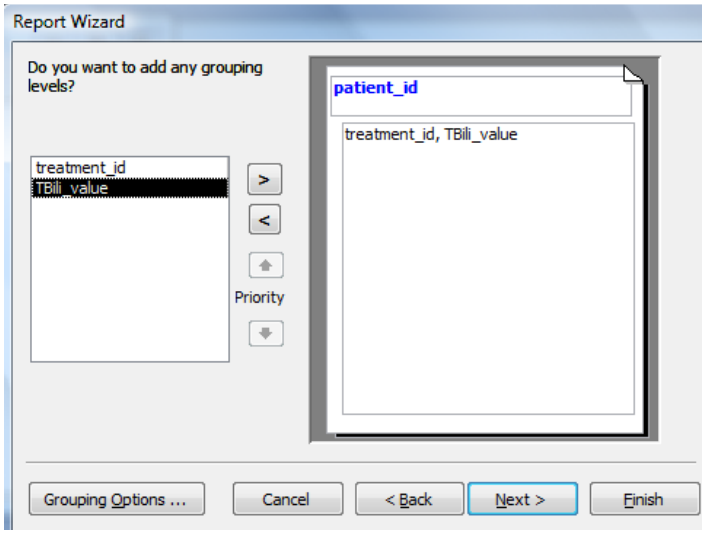


Figure 20. Choosing a grouping level for a new report.

Data was then decided to be sorted by date, in ascending order. This would provide a report showing, for example, all lab data for a particular patient from the first set of labs obtained to the most recent (Fig. 21).

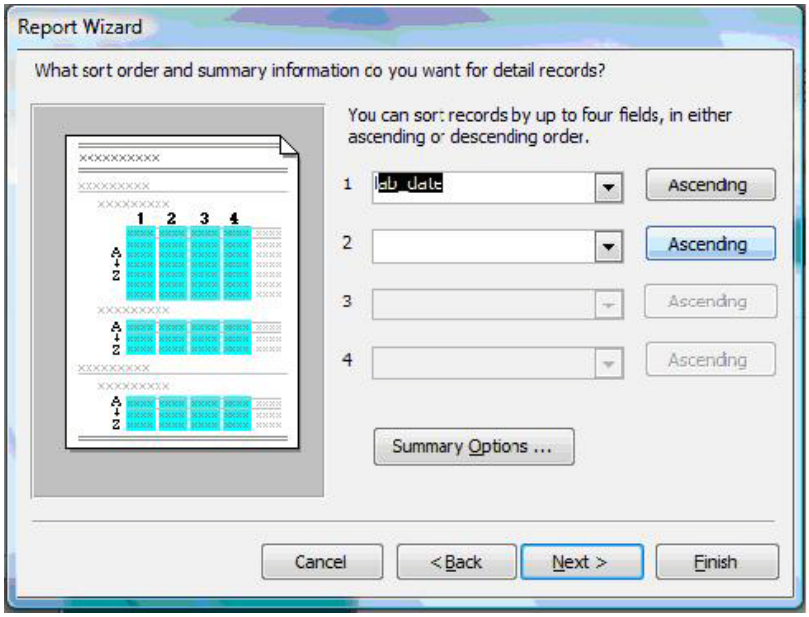


Figure 21. Designing data output format for a report.

The final step was to choose the report view layout (Fig. 22), where the stepped view in landscape format was chosen for this application. To allow ease of use in report formation with data extracted by the queries was to create a form called Report Builder. This form allows the user to enter a patient ID and view either the patient demographics or lab values and treatment details, and is accessible from the main switchboard (Fig. 23) by selecting "View Patient Reports" (Fig. 24).

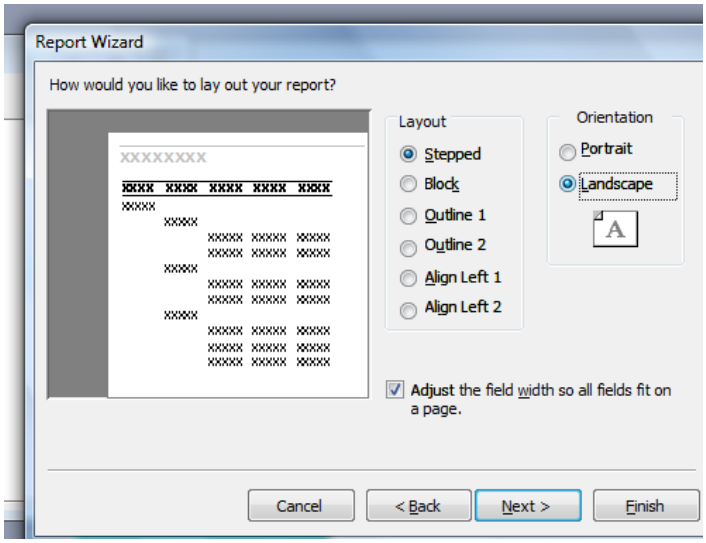


Figure 22. Choosing a report layout format.

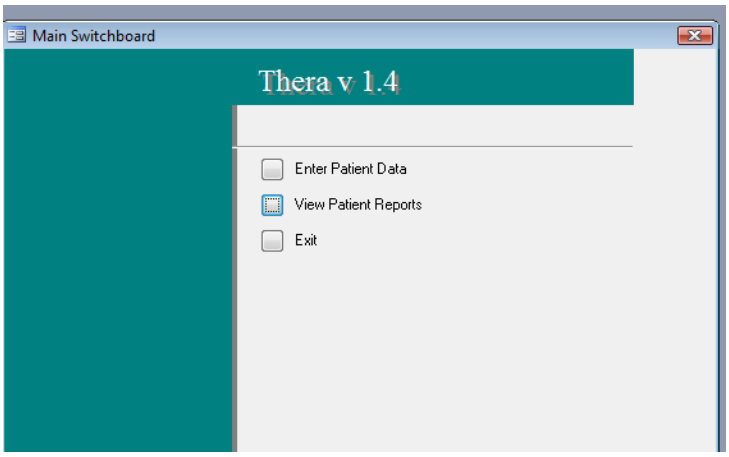


Figure 23. Accessing the Report Builder form from the Main Switchboard.

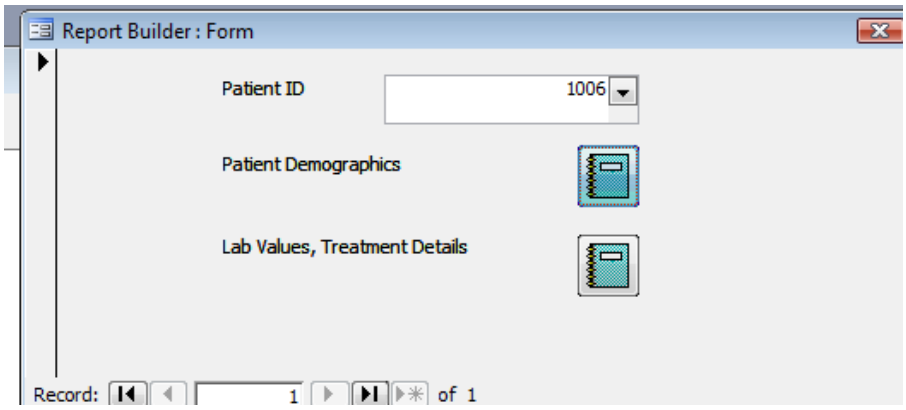


Figure 24. Building a report from the Report Builder form.

The resulting report for the patient demographic selection is displayed (Fig. 25)

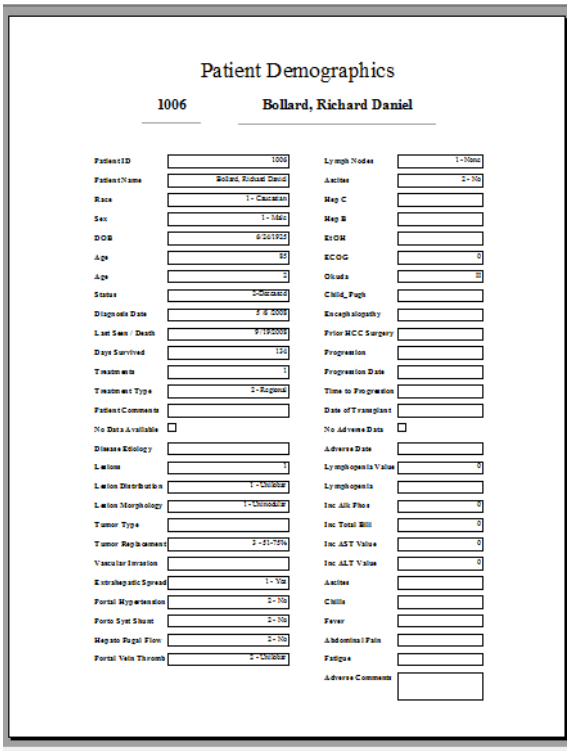


Figure 25. Final report layout from the Report Builder form accessible through the Main Switchboard.

Two options are now available for preparing reports for patient data. The user may go through the main switchboard which is displayed on startup and click on the "patient reports" box, or may go to the reports section in the main MS Access navigation pane and choose a report to be displayed. From that screen, a window requesting the patient ID is displayed (Fig. 26).

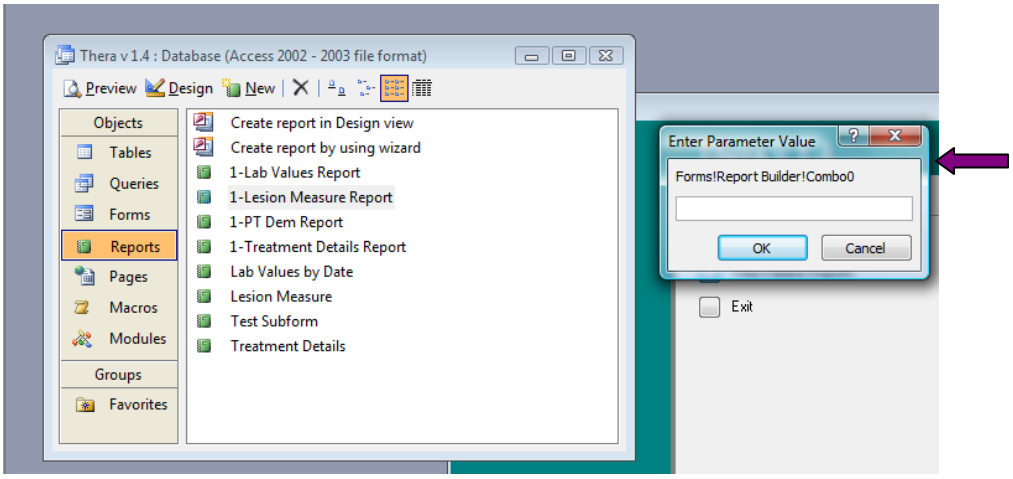


Figure 26. Building a report from the MS Access main console.

Following input of the patient ID, the report will utilize the appropriate query to prepare the output (in the case of "lab values report) shown in Fig. 27.

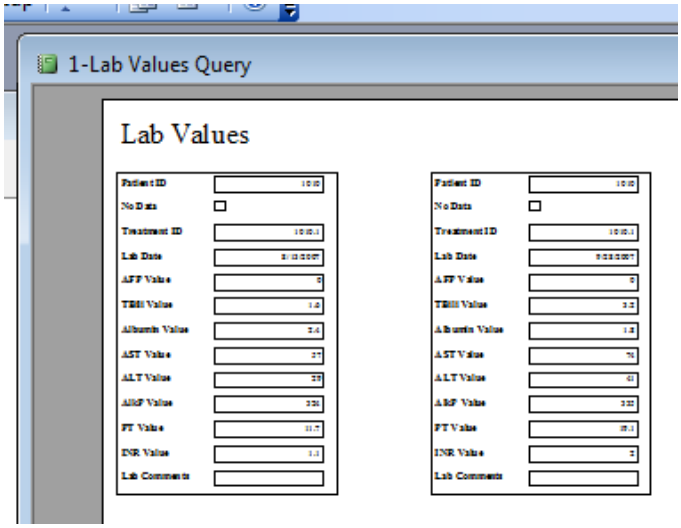


Figure 27. Lab values report prepared via the MS Access main console

Results

The resulting HCC database allows for ease of use in entering and accessing data for patients treated for HCC. From a user standpoint, two simple steps are required to reach the patient data entry forms. After opening the database, the user clicks on the "Enter patient data" box from the main switchboard. The user then tabs to one past the last record to find the first available blank record, enters data, and clicks the "save and close" button when data entry is completed (Fig. 28).

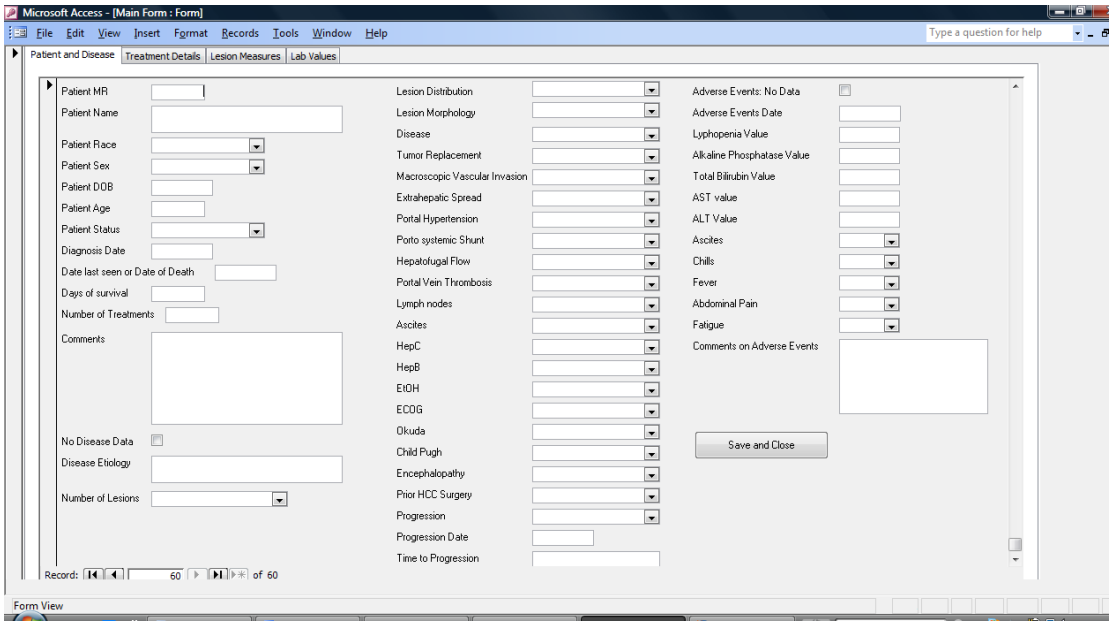


Figure 28. The main data entry form accessible from the HCC database main switchboard.

When preparing reports, the user has a variety of options, the most straightforward of which is to choose the "View patient reports" option from the main switchboard, enter a patient ID number, and have reports automatically generated through the queries which access specific data from the tables. All that the user sees is a final, formatted version of a report containing the data they wish to see for a particular patient (Fig. 29).

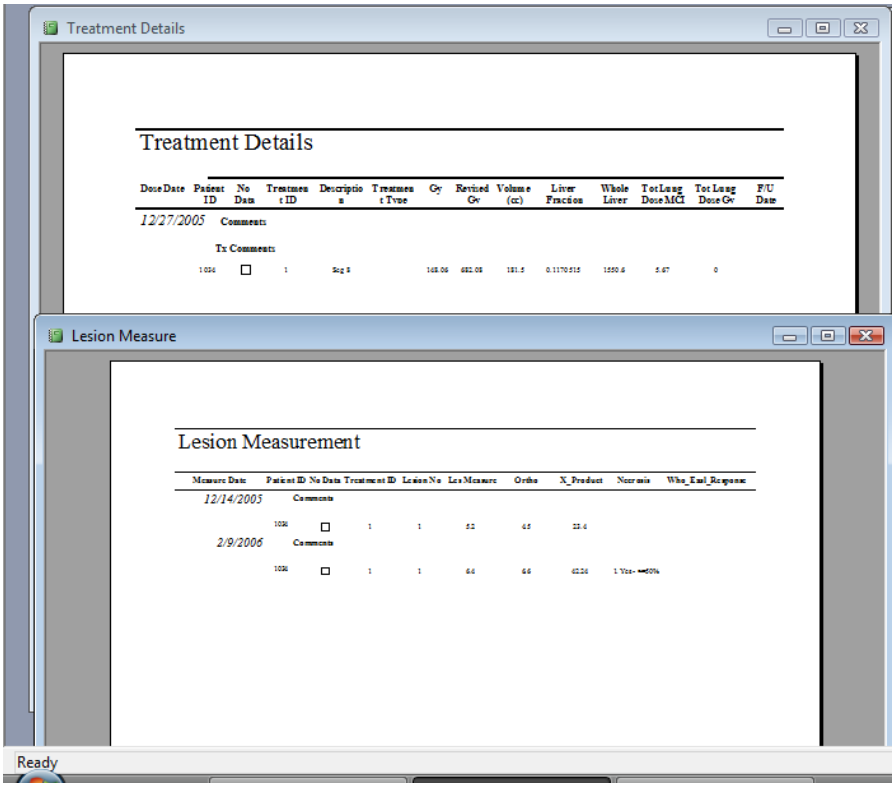


Figure 29. Examples of final reports generated via the HCC database main switchboard.

Discussion, future directions and conclusion

The HCC database provides a secure method of data entry and report generation for patients undergoing treatment for HCC at BGS Medical Center. The database is in effect password protected as it is located on a shared drive accessible only by BGS employees with password access to that drive. The database is currently in use, and all the original records which were missing some data points have been completely filled in by manual searches for data at the BGS liver center. Presently, data is entered for each patient by the

Interventional Radiology staff as the patient is undergoing treatment to assure completeness of each record.

Ideally, when system for data storage and manipulation is replaced by another, analyses would be performed to measure improvements in the system. Since the original data storage system consisted of hand written records, and then progressed to records stored in multiple MS Excel files with no measurement of variables such as reduction of complication rates or errors in either system, it is difficult to find comparable variables which could be measured for this type of analysis. Clearly the time to locate a specific file is much shorter with the current database, as the user only needs to type in a patient name and all information for that patient is immediately available. Additionally, the time to compile a report of all patients who have received a specific therapy, for example, would take much longer in either of the previous systems while this information can be accessed in seconds through the new database by using an existing query. A subjective report in improvement has been made is through surveying the people who use the system on a day-to-day basis, in this case, informal reports from users are overwhelmingly positive regarding ease of use of the database and perceived time saved.

Creating data repositories such as this HCC database have obvious implications for future research. Given the information in this database, analyses such as comparison of treatment response for different treatments, treatment response for patients with differences in initial pathology, and comparison of adverse events for different treatments can be performed. Future projects may address, for

example, comparison of tumor reduction in patients receiving RFA vs. TACE, or TACE vs. radio-embolization. Another project might compare patients with different initial pathology (HBV vs. HCV vs. Hemochromatosis) who all receive TACE. Finally, a study comparing adverse outcomes for each procedure may be critical in helping guide this relatively new field of therapies. Lastly, data such as pathology reports from biopsies and tumor excision may be included in this database in the future, allowing for the possibility of comparing treatments for specific molecular and genetic profiles of each tumor.

The HCC database allows for ease of data entry, simplicity of data extraction, and also data sharing. For example, if there is interest in pursuing multi-center research, all of the data may now easily be shared with participating institutions through reports or even transfer of the entire database.

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Development of a Database for Storage and Analysis of Factors Affecting Treatment of Hepatocellular Carcinoma

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Abstract

Hepatocellular carcinoma (HCC) is the fifth most common solid tumor worldwide. There are 626,000 new cases per year of primary liver cancer worldwide, most of which are HCC. Over 1,000,000 people die of HCC per year, making HCC the third most frequent cause of cancer deaths worldwide(1). The standard treatment for HCC is surgical resection, however on presentation many patients have progressed to the point where such treatment is not an option, and are placed on liver transplant lists. Palliative treatment modalities are often used in the interim, including trans-arterial chemoembolization (TACE), radiofrequency ablation (RFA), or systemic chemotherapy. In this study over 200 patients who received either Therasphere or Sirsphere (TACE methods), or RFA treatment for unresectable HCC were catalogued in a relational database allowing for analysis of treatment outcomes and treatment comparisons. A Microsoft Access database was created to store data such as patient demographics, disease details, adverse events, patient lab values, treatment details, and pre- and post-lesion measurements. This database is currently in use by the department of Interventional Radiology at Banner Good Samaritan Medical Center.

Database population

The initial set of data for this project was collected by hand by Dr. David Wood and compiled by members of the Interventional Radiology department at Banner Good Samaritan hospital in a Microsoft Excel file. This method of data entry was cumbersome and did not allow the production of reports for a particular patient or particular set of variables. The original data was extracted manually from patient medical records, from records in the BGS liver center, and from observations made during IR procedures.

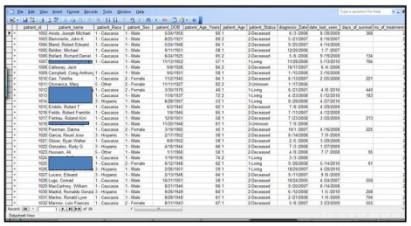

Figure 1: Construction of data tables for HCC database

Data stored in HCC database

Patient demographics including race, sex, age, diagnosis date, current status (living or deceased), days of survival, number of interventional radiology treatments, treatment type(s), disease etiology, lesion distribution and morphology, characteristics of the disease such as presence of ascites, portal vein thrombosis, etc, as well as standard prognostic scores including Okuda, Child-Pugh and ECOG are stored in the HCC database.
Lab values, including α-fetoprotein levels, AST, ALT, alkaline phosphatase, albumin, total bilirubin, PT and INR are stored for each patient. Pre- and post-treatment lesion measures and degree of necrosis are listed for each tumor in each patient. Treatment details including radiation dose date, dose, and region of distribution are also recorded.

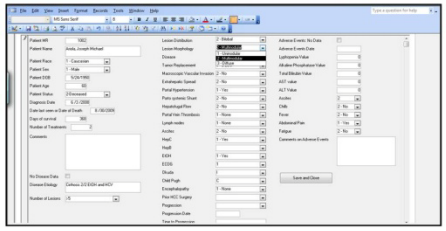

Figure 2: Construction of forms for data viewing and data entry

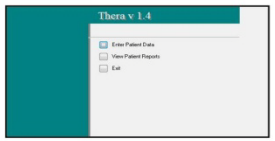

Figure 3: Main switchboard

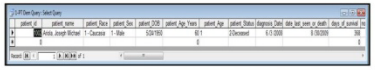

Figure 5: Result of query in table form

Database construction

Tables containing related data were constructed in MS Access. For example, a table containing patient demographics, variables related to disease description, and recorded adverse events stored multiple points of data per patient (Figure 1). Corresponding forms to the data tables were constructed, allowing ease of viewing of the data stored in the tables as well as data entry (Figure 2). A main switchboard form was created to act as an initial point for data entry/editing and preparing patient reports (Figure 3). Queries were then created which extracted desired data from data tables to be presented in reports. For example, if the user desired to view treatment details and lesion measurement data for a patient, the queries would extract relevant data and present them in report form (Figure 5). Results of queries may also be presented in table form (Figure 4).

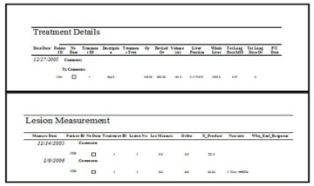

Figure 4: result of query in report form

Discussion

The HCC database allows for ease of use in entering and accessing data for patients treated for HCC. From a user standpoint, two simple steps are required to reach the patient data entry forms. After opening the database, the user clicks on the "Enter patient data" box from the main switchboard. The user then tabs to the first available blank record, enters data, and clicks the "save and close" button when data entry is completed. The HCC database provides a secure method of data entry and report generation for patients undergoing treatment for HCC at BGS Medical Center. The database is in effect password protected as it is located on a shared drive accessible only by BGS employees with password access to that drive. Data is entered for each patient by the Interventional Radiology staff as the patient is undergoing treatment. Creating data repositories such as this HCC database have significant implications for future research. Given the information in this database, analyses such as comparison of treatment response for different treatments, treatment response for patients with differences in initial pathology, and comparison of adverse events for different treatments can be performed. Additionally, the stored information may be shared with other institutions for pursuing multi-center research. As pathology specimens are stored for each patient by the pathology department, the possibility of comparing treatments on specific molecular and genetic profiles of each tumor might also be pursued.

References

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2. Burak KW et al.: An evidence-based multidisciplinary approach to the management of hepatocellular carcinoma (HCC): the Alberta HCC algorithm. Can J Gastroenterol 24(11):643-50 (2010)